

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2003/Feb W3

(c) format only 2003 The Dialog Corp.

File 55:Biosis Previews(R) 1993-2003/Feb W3

(c) 2003 BIOSIS

*File 55: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 34:SciSearch(R) Cited Ref Sci 1990-2003/Feb W3

(c) 2003 Inst for Sci Info

*File 34: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 340:CLAIMS(R)/US Patent 1950-03/Feb 20

(c) 2003 IFI/CLAIMS(R)

*File 340: The Claims U.S. Patent databases have been reloaded.

HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.

Set	Items	Description
? s prevent?	(5n)	(cancer or tumor or carcinoma or malignan?)
	1775210	PREVENT?
	1166376	CANCER
	1274207	TUMOR
	722566	CARCINOMA
	483393	MALIGNAN?
S1	39262	PREVENT? (5N) (CANCER OR TUMOR OR CARCINOMA OR MALIGNAN?)
? s lymphocyte??		
S2	678612	LYMPHOCYTE??
? s s1 and s2		
	39262	S1
	678612	S2
S3	1558	S1 AND S2
? s cd(w)3 or cd3 or okt3 or okt(w)3 or interleukin(w)2		
Processing		
Processing		
	150106	CD
	8814403	3
	1190	CD(W)3
	54996	CD3
	7507	OKT3
	1239	OKT
	8814403	3
	518	OKT(W)3
	373138	INTERLEUKIN
	10337636	2
	108074	INTERLEUKIN(W)2
S4	157862	CD(W)3 OR CD3 OR OKT3 OR OKT(W)3 OR INTERLEUKIN(W)2
?		
? s s3 and s4		
	1558	S3
	157862	S4
S5	283	S3 AND S4
? s s5 and py<=2001		
Processing		
Processing		
Processing		
	283	S5
	40185934	PY<=2001
S6	250	S5 AND PY<=2001
? s year??		
S7	2121826	YEAR??
? s s6 and s7		

250 S6
2121826 S7
S8 7 S6 AND S7

? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.

...completed examining records

S9 7 RD (unique items)

? t s9/3,k,ab/1-7

9/3,K,AB/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

08412769 95178434 PMID: 7873494

Prevention of cancer recurrence by infusion of activated autologous lymphocytes]

Sekine T; Takayama T; Konomi Y; Kakizoe T

National Cancer Center Research Institute, Tokyo, Japan.

Human cell : official journal of Human Cell Research Society (JAPAN)

Sep 1994, 7 (3) p121-4, ISSN 0914-7470 Journal Code: 8912329

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: Completed

Activated and expanded autologous peripheral blood **lymphocytes** by cultivation with immobilized anti-**CD3** antibody and IL-2 have been infused to the patients with hepatocellular carcinoma after culative operation as a randomized clinical trial. This study is on-going and primary efficacy endpoints of this study were disease-free survival and overall survival, and the sample size for the study was designed as a minimum of 146 patients. From interim analysis at the second **year** from start of the study, Eligible cases were 101, 49 cases in treated group and 52 cases in control. Recurrences were confirmed 13 cases from treated group and 22 cases from control group. Minor adverse reaction were observed in 28 cases (57%).

Prevention of cancer recurrence by infusion of activated autologous lymphocytes]

Sep 1994,

Activated and expanded autologous peripheral blood **lymphocytes** by cultivation with immobilized anti-**CD3** antibody and IL-2 have been infused to the patients with hepatocellular carcinoma after culative...

... study was designed as a minimum of 146 patients. From interim analysis at the second **year** from start of the study, Eligible cases were 101, 49 cases in treated group and...

Descriptors: Carcinoma, Hepatocellular--therapy--TH; *Immunotherapy, Adoptive--methods--MT; *Liver Neoplasms--therapy--TH; ***Lymphocytes** --immunology--IM; Antibodies, Monoclonal--immunology--IM; Antigens, **CD3**--immunology--IM; **Interleukin-2**--pharmacology--PD; Killer Cells--immunology--IM; **Lymphocyte** Transformation

Chemical Name: Antibodies, Monoclonal; Antigens, **CD3**; **Interleukin-2**

9/3,K,AB/2 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

06257375 Genuine Article#: YE747 Number of References: 142

Title: Recent advances in the treatment of malignant melanoma with gene

med Abstracts
2/25

therapy (ABSTRACT AVAILABLE)

Author(s): Hersh EM (REPRINT) ; Stopeck AT

Corporate Source: UNIV ARIZONA, ARIZONA CANC CTR, 1515 N CAMPBELL AVE, POB 245024/TUCSON/AZ/85724 (REPRINT)

Journal: MOLECULAR MEDICINE, 1997, V3, N10 (OCT), P636-651

ISSN: 1076-1551 Publication date: 19971000

Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010

Language: English Document Type: REVIEW

Abstract: Malignant melanoma is a growing problem. In 1997 there will be in excess of 40,000 cases of malignant melanoma in the United States, with 7300 deaths occurring (1). The incidence has been increasing by 5% per year for the last 40 years. Interestingly, the survival rate has also improved by almost 5% per year (2). The overall survival rate has gone from 60% to over 80% during this period. The prognostic variables that predict for a high likelihood of relapse among patients with primary cutaneous melanoma or regional lymph nodes recurrences are well established (3). Thus, there are well-defined groups of patients who can be targeted for biological therapy and gene therapy to prevent relapse. The immunological characteristics of malignant melanoma have been studied extensively and can be used to develop approaches to immunotherapy (4). Tumor-associated or tumor-specific antigens have been described at the molecular level (5). These can induce specific cytotoxic T cell (CTL) and antibody responses. This natural immune reactivity has provided the foundation for biological and gene therapy of melanoma. There is also abundant data that both general immunocompetence and specific immune reactivity to melanoma predict for a good prognosis (6). Recently, molecular mechanisms have been described that explain how melanoma and other cancers evade the immune response and why anti-tumor host defense mechanisms fail. These provide additional targets for biological and gene therapy of melanoma.

, 1997

...Abstract: United States, with 7300 deaths occurring (1). The incidence has been increasing by 5% per year for the last 40 years. Interestingly, the survival rate has also improved by almost 5% per year (2). The overall survival rate has gone from 60% to over 80% during this period...

...defined groups of patients who can be targeted for biological therapy and gene therapy to prevent relapse. The immunological characteristics of malignant melanoma have been studied extensively and can be used to develop approaches to immunotherapy (4

...Identifiers--TUMOR-INFILTRATING LYMPHOCYTES; ACTIVE-SPECIFIC IMMUNOTHERAPY; COLONY-STIMULATING-FACTOR; CYTOLYTIC T-LYMPHOCYTES ; CELL-SURFACE ANTIGENS; NATURAL-KILLER-CELLS; INTERLEUKIN-2 GENE; IN-VIVO; BIOLOGICAL PROPERTIES; METASTATIC MELANOMA

Research Fronts: 95-1687 006 (CYTOLYTIC T-LYMPHOCYTES; HUMAN-MELANOMA ANTIGEN GP100; PRIMARY CTL RESPONSES; TYROSINASE GENES; RECOGNITION OF MULTIPLE EPITOPES; CANCER VACCINES...

9/3,K,AB/3 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

05720818 Genuine Article#: WT283 Number of References: 14

Title: Risk of malignancy in pediatric renal transplant recipients. (ABSTRACT AVAILABLE)

Author(s): Gagnadoux MF (REPRINT)

Corporate Source: HOP NECKER ENFANTS MALAD, SERV NEPHROL PEDIAT, 149 RUE SEVRES/F-75743 PARIS 15//FRANCE/ (REPRINT)

Journal: ANNALES DE PEDIATRIE, 1997, V44, N3 (MAR), P187-192

ISSN: 0066-2097 Publication date: 19970300

Publisher: EXPANSION SCI FRANCAISE, 31 BLVD LATOUR MAUBOURG, 75007 PARIS, FRANCE

Language: French Document Type: REVIEW

Abstract: Factors that may account for the increased risk of malignant disease in allograft recipients include antigenic stimulation by the allograft, reactivation of oncogenic viruses, and depletion of natural killer **lymphocytes**. In adults, malignancies complicate about 5% of renal transplantations, and the risk of cancer approximates 10% after ten **years**. The most common malignancies are skin cancer (40%), which occur after a mean of ten **years**; lymphoproliferative disorders (LPD, 15%), after a mean of 33 months; Kaposi's sarcoma, after a mean of 20 months; and vulvoperineal carcinomas complicating condylomatosis, after a mean of 12 **years**. In children, only about 1% of transplant procedures are followed by development of a malignancy, which is an LPD in 27 to 75% of cases. In a study of 873 kidney transplants performed in subjects younger than 18 **years**, the incidence of malignancy was 0.8%, versus 6.9% in 43 patients who were older than 18 **years** at transplantation. Of the ten malignancies in the pediatric group, two were LPDs (20%), two were liver carcinomas complicating hepatitis B or C, two were Kaposi's sarcomas, one was a urinary bladder carcinoma after long-term cyclophosphamide therapy, one was a carcinoma of the vulva and cervix, and two were unclassified tumors of the meninges and ovary. None of the pediatric patients developed skin cancer, although follow-up was longer than ten **years** in 157 patients. Half the malignancies were fatal (one LPD, one Kaposi's sarcoma, the two liver cancers and the bladder cancer). One or more risk factors were identified in seven of the ten patients, including oncogenic viruses (HBV, HCV, EBV, HPV) severe immunodepression (OKT3++), and a history of oncogenic chemotherapy. **Prevention of malignancies** in renal transplant recipients currently relies on caution in the use of immunosuppressants and early detection of premalignant lesions, and in the future may benefit from the development of antiviral drugs.

, 1997

- ...Abstract: include antigenic stimulation by the allograft, reactivation of oncogenic viruses, and depletion of natural killer **lymphocytes**. In adults, malignancies complicate about 5% of renal transplantations, and the risk of cancer approximates 10% after ten **years**. The most common malignancies are skin cancer (40%), which occur after a mean of ten **years**; lymphoproliferative disorders (LPD, 15%), after a mean of 33 months; Kaposi's sarcoma, after a mean of 20 months; and vulvoperineal carcinomas complicating condylomatosis, after a mean of 12 **years**. In children, only about 1% of transplant procedures are followed by development of a malignancy...
- ...of cases. In a study of 873 kidney transplants performed in subjects younger than 18 **years**, the incidence of malignancy was 0.8%, versus 6.9% in 43 patients who were older than 18 **years** at transplantation. Of the ten malignancies in the pediatric group, two were LPDs (20%), two...
- ...None of the pediatric patients developed skin cancer, although follow-up was longer than ten **years** in 157 patients. Half the malignancies were fatal (one LPD, one Kaposi's sarcoma, the...
- ...in seven of the ten patients, including oncogenic viruses (HBV, HCV, EBV, HPV) severe immunodepression (OKT3++), and a history of oncogenic chemotherapy. **Prevention of malignancies** in renal transplant recipients currently relies on caution in the use of immunosuppressants and early...

9/3,K,AB/4 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

04594109 Genuine Article#: TV846 Number of References: 26

Title: BETA-CAROTENE SUPPLEMENTATION ENHANCES **LYMPHOCYTE**
-PROLIFERATION WITH MITOGENS IN HUMAN PERIPHERAL-BLOOD
LYMPHOCYTES (Abstract Available)

Author(s): MORIGUCHI S; OKISHIMA N; SUMIDA S; OKAMURA K; DOI T; KISHINO Y
Corporate Source: UNIV TOKUSHIMA,SCH MED,DEPT NUTR/TOKUSHIMA 770//JAPAN/;
OSAKA GAKUIN UNIV/OSAKA 564//JAPAN/; OTSUKA PHARMACEUT CO LTD,SAGA RES
INST/SAGA 84201//JAPAN/

Journal: NUTRITION RESEARCH, 1996, V16, N2 (FEB), P211-218

ISSN: 0271-5317

Language: ENGLISH Document Type: ARTICLE

Abstract: This study was performed to determine the effect of beta-carotene supplementation on the proliferation of human peripheral blood **lymphocytes** (PBL) with T-cell mitogens such as phytohemagglutinin (PHA) and concanavalin A (Con A). Subjects were healthy male university students (19 to 22 **years** old) without smoking habit. After the subjects were divided into two groups; control (n=7) and beta-carotene supplemented (n=8) groups, they received lactose (30 mg/day) and beta-carotene (30 mg/day) for 30 days, respectively. Their peripheral blood **lymphocytes** (PBL) were separated by Percoll-density gradient centrifugation and used for immunological assays. The number of PBL from beta-carotene supplemented group was not significantly different from control group. Although there was also no significant difference in natural killer cell (NK) activity between both groups (Control; 33.4 +/- 8.2%, beta-carotene; 32.5 +/- 7.7%), proliferation of PBL with PHA or ConA was 1.4 to 1.9 fold higher in beta-carotene supplemented group compared to that of control group. However, the proportions of T cell subsets in PBL and **interleukin 2** (IL2) activity in the supernatant of PBL cultures stimulated in vitro with Con A were not significant differences between control and beta-carotene supplemented groups. In particular, IL2 activity was lower in beta-carotene supplemented subjects compared to that of control subjects. These results suggest that the enhancement of PBL proliferation following beta-carotene supplementation is not due to the qualitative change in T cell subsets of PBL and the increase in IL2 production as T cell growth factor but due to the enhancement in the responsiveness of PBL to mitogen.

Title: BETA-CAROTENE SUPPLEMENTATION ENHANCES **LYMPHOCYTE**
-PROLIFERATION WITH MITOGENS IN HUMAN PERIPHERAL-BLOOD
LYMPHOCYTES

, 1996

...Abstract: to determine the effect of beta-carotene supplementation on the proliferation of human peripheral blood **lymphocytes** (PBL) with T-cell mitogens such as phytohemagglutinin (PHA) and concanavalin A (Con A). Subjects were healthy male university students (19 to 22 **years** old) without smoking habit. After the subjects were divided into two groups; control (n=7...

...mg/day) and beta-carotene (30 mg/day) for 30 days, respectively. Their peripheral blood **lymphocytes** (PBL) were separated by Percoll-density gradient centrifugation and used for immunological assays. The number...

...to that of control group. However, the proportions of T cell subsets in PBL and **interleukin 2** (IL2) activity in the supernatant of PBL cultures stimulated in vitro with Con A were...

...Research Fronts: IN-VITRO; DISSEMINATED INFECTION; CRUISE SHIP)
94-3520 001 (METABOLISM OF BETA-CAROTENE; ANTIOXIDANT ACTIVITY;
CANCER PREVENTION; ADULT WOMEN; CIS-TRANS ISOMERIZATION)

9/3,K,AB/5 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

03840060 Genuine Article#: QK660 Number of References: 71
Title: MEDITATION, MELATONIN AND BREAST PROSTATE-CANCER - HYPOTHESIS AND
PRELIMINARY DATA (Abstract Available)
Author(s): MASSION AO; TEAS J; HEBERT JR; WERTHEIMER MD; KABATZINN J
Corporate Source: UNIV MASSACHUSETTS, MED CTR, DEPT PSYCHIAT, 55 LAKE AVE
N/WORCESTER//MA/01655
Journal: MEDICAL HYPOTHESES, 1995, V44, N1 (JAN), P39-46
ISSN: 0306-9877
Language: ENGLISH Document Type: ARTICLE
Abstract: The objective of this study was to test the hypothesis that the
regular practice of mindfulness meditation is associated with increased
physiological levels of melatonin. Melatonin may be related to a
variety of biologic functions important in maintaining health and
preventing disease, including breast and prostate **cancer**.
Previous studies have shown melatonin production is photosensitive and
we suggest here that it also may be psychosensitive.

A cross-sectional study of 12-hour (20:00 - 08:00) urinary
6-sulphatoxymelatonin was conducted from which we analyzed data from 8
women who regularly meditate (RM) and 8 women who do not meditate (NM).
All samples were collected in the homes of study participants.
Volunteers were recruited to provide 12-hour overnight samples of
urine. All subjects collected the samples on one night during the same
1-week period. There was no explicit intervention. However, all RM were
either graduates of, or teachers in, the University of Massachusetts
Stress Reduction and Relaxation Program.

The main outcome measure was the total excretion of urinary
6-sulphatoxymelatonin. Multiple linear regression (Proc GLM in SAS) was
performed to test the effect of meditation (RM vs NM) on
6-sulphatoxymelatonin.

The results of the study were that after controlling for the
non-significant effect of menstrual period interval, we found an effect
of meditation group (RM vs NM: $b = 1.983$; $F = 6.78$; $p = 0.02$) and age
(for each integer **year**: $b = -0.169$; $F = 8.41$; $p = 0.01$). The
conclusion is that study results are consistent with our hypothesis and
indicate that melatonin might be a useful parameter in testing similar
psyche-social interventions. Given that two intervention studies have
provided support for the concept of psycho-physiological interactions
in survival among cancer patients, applications of our findings might
be pertinent to the area of breast and prostate cancer.

, 1995

...Abstract: Melatonin may be related to a variety of biologic functions
important in maintaining health and **preventing** disease, including
breast and prostate **cancer**. Previous studies have shown melatonin
production is photosensitive and we suggest here that it also...

...NM: $b = 1.983$; $F = 6.78$; $p = 0.02$) and age (for each integer **year**:
 $b = -0.169$; $F = 8.41$; $p = 0.01$). The conclusion is that study results...

...Identifiers--VASOACTIVE-INTESTINAL-PEPTIDE; PINEAL HORMONE MELATONIN;
MALIGNANT-MELANOMA; HUMAN-LYMPHOCYTES; GLAND; CELLS; SECRETION;
6-SULFATOXYMELATONIN; **INTERLEUKIN-2**; MODULATION

9/3,K,AB/6 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

03195398 Genuine Article#: NM330 Number of References: 38
Title: HUMAN LUNG-TUMOR CELL SECRETION OF **INTERLEUKIN-2** FOR
 PROTECTION AGAINST TUMOR ENGRAFTMENT (Abstract Available)
Author(s): ALOSCO T; GANSBACHER B; BANKERT R; TAKITA H; PETRELLI N
Corporate Source: ROSWELL PK CANC INST,DEPT SURG ONCOL,ELM & CARLTON
 ST/BUFFALO//NY/14263; ROSWELL PK CANC INST,DEPT MOLEC
 IMMUNOL/BUFFALO//NY/14263; MEM SLOAN KETTERING CANC CTR,DEPT
 HEMATOL/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR,DEPT
 LYMPHOMA/NEW YORK//NY/10021

Journal: ANNALS OF SURGICAL ONCOLOGY, 1994, V1, N3 (MAY), P229-235

ISSN: 1068-9265

Language: ENGLISH Document Type: ARTICLE

Abstract: Background: Lung cancer continues to claim large numbers of human
lives each **year** despite advances made in conventional therapies.

The use of biologic response modifiers to modulate the immune system
against human tumors is an alternate form of immunotherapy.

Interleukin-2 (IL-2), or T-cell growth factor, is an
important modulator of activated T cells. We show here that tumor cells
transduced with human IL-2 cDNA provide protective immunity against
engraftment of IL-2-secreting, as well as parental non-IL-2-secreting,
tumor cells in vivo.

Methods: In an attempt to increase the antigen-induced
proliferation and cytotoxicity T cells within the vicinity of tumor
antigen, we have transduced human lung tumor cell lines (generated from
whole tumor specimens obtained fresh from the operating room) with a
vector containing the IL-2 gene. Cell lines secreting 0.5-20 Cetus
units/ml of IL-2 were generated. Control cell lines were similarly
established using the same retroviral vector containing the gene for
adenosine deaminase (ADA). The growth of tumor xenografts of the
vector-modified cell lines was observed in severe combined
immunodeficient (scid) mice.

Results: Using C.B-17 scid mice, we have observed that the local
secretion of IL-2 by these human lung **tumor** cell lines will
prevent engraftment of that **tumor** into scid mice. The
parental tumor as well as the tumor containing the ADA gene grow
aggressively in the scid mouse. Growth arrest also correlated strongly
with the amount of IL-2 secreted by the tumor cells. The local
secretion of IL-2 by the transduced cell line will abrogate the
tumorigenicity of the parental cell line as well as an allogeneic
tumor. The inhibition of growth occurs only when the tumors are placed
in close proximity to each other. After gamma irradiation, transduced
tumor cells will continue to secrete IL-2.

Conclusion: These results indicate that (a) human lung tumor cell
lines can be transduced with IL-2-containing retroviral vectors; (b)
local and sustained release of IL-2 will induce an antitumor response
by the host against the IL-2-secreting as well as the control tumor
cells; (c) secretion of IL-2 continues after the cells are irradiated.
This study suggests that cytokine-secreting human lung tumors may be
used in vaccination protocols for cancer patients.

Title: HUMAN LUNG-TUMOR CELL SECRETION OF **INTERLEUKIN-2** FOR
 PROTECTION AGAINST TUMOR ENGRAFTMENT
 , 1994

Abstract: Background: Lung cancer continues to claim large numbers of human
lives each **year** despite advances made in conventional therapies.

The use of biologic response modifiers to modulate the immune system
against human tumors is an alternate form of immunotherapy.

Interleukin-2 (IL-2), or T-cell growth factor, is an
important modulator of activated T cells...

...mice, we have observed that the local secretion of IL-2 by these human
lung **tumor** cell lines will **prevent** engraftment of that

tumor into scid mice. The parental tumor as well as the tumor containing the ADA gene...

...Identifiers--SEVERE COMBINED IMMUNODEFICIENCY; ACTIVATED KILLER CELLS; MEDIATED GENE-TRANSFER; INFILTRATING **LYMPHOCYTES**; RECOMBINANT **INTERLEUKIN-2**; ADOPTIVE IMMUNOTHERAPY; ANTITUMOR RESPONSE; INTERFERON-GAMMA; ADVANCED CANCER; MELANOMA-CELLS

Research Fronts: 92-1406 003 (RECOMBINANT **INTERLEUKIN-2** IN METASTATIC RENAL-CELL CARCINOMA; ADOPTIVE IMMUNOTHERAPY OF CANCER; TUMOR INFILTRATING **LYMPHOCYTES**)

92-2548 002 (SCID MICE; SEVERE COMBINED IMMUNODEFICIENT (SCID) MOUSE; ECTOPIC LYMPHOKINE GENE-EXPRESSION IN HUMAN PERIPHERAL-BLOOD **LYMPHOCYTES** INVIVO)

92-5364 002 (INVIVO GENE-TRANSFER; LOCAL IMMUNOTHERAPY OF CANCER; IL-2 EXPRESSION; REDUCED TUMORIGENICITY; MURINE MELANOMA; MOUSE **LYMPHOCYTES**-T; ANTIGEN PRESENTATION)

92-0504 001 (EXPRESSION OF GELATINASE TYPE-IV COLLAGENASE; METALLOTHIONEIN INDUCTION; TISSUE...

9/3,K,AB/7 (Item 6 from file: 34)
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
 (c) 2003 Inst for Sci Info. All rts. reserv.

01857745 Genuine Article#: JG513 Number of References: 24
 Title: REDUCED TENASCIN EXPRESSION IN COLONIC-CARCINOMA WITH LYMPHOGENOUS METASTASIS (Abstract Available)
 Author(s): SUGAWARA I; HIRAKOSHI J; MASUNAGA A; ITOYAMA S; SAKAKURA T
 Corporate Source: SAITAMA MED SCH,SAITAMA MED CTR,DEPT PATHOL,1981 KAMODA TSUJIDO CHO/KAWAGOE/SAITAMA 350/JAPAN/; RIKEN,CELL BIOL LAB/TSUKUBA/IBARAKI/JAPAN/
 Journal: INVASION & METASTASIS, 1991, V11, N6 (NOV-DEC), P325-331
 Language: ENGLISH Document Type: ARTICLE
 Abstract: We have studied expression of tenascin (TN) in colonic carcinoma cells from 81 patients with colonic carcinoma without (20) and with (61) lymphogenous metastases, in order to assess whether TN plays a role in local invasiveness and metastasis of tumors. In metastatic colonic carcinoma tissues from 52 cases, moderate, partial expression of TN was observed in the primary foci but no TN expression was observed in tissues from 9 others. However, in every case of nonmetastatic colonic carcinoma, very strong TN expression was observed in the tissues. Furthermore, the presence of dense TN accumulation correlated well with the prognoses (1-year survival) of colonic cancer patients ($p < 0.01$). Weak TN expression was observed in 24/61 of the metastatic lymph nodes examined. In 2 patients with metastatic colonic carcinoma, the colonic cancer cells produced TN. TN may, therefore, play a role in limiting or **preventing** local **tumor** invasion rather than **preventing** metastasis and is a useful marker for predicting the prognoses of patients with colonic cancer.

, 1991

...Abstract: the tissues. Furthermore, the presence of dense TN accumulation correlated well with the prognoses (1-year survival) of colonic cancer patients ($p < 0.01$). Weak TN expression was observed in 24...

...the colonic cancer cells produced TN. TN may, therefore, play a role in limiting or **preventing** local **tumor** invasion rather than **preventing** metastasis and is a useful marker for predicting the prognoses of patients with colonic cancer.

Research Fronts: 90-0093 001 (RECOMBINANT **INTERLEUKIN-2**; LYMPHOKINE-ACTIVATED KILLER-CELLS; TUMOR-INFILTRATING **LYMPHOCYTES**; CANCER-PATIENTS RECEIVING ADOPTIVE IMMUNOTHERAPY)

?

YSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2003/Feb W3

(c) format only 2003 The Dialog Corp.

File 55:Biosis Previews(R) 1993-2003/Feb W3

(c) 2003 BIOSIS

*File 55: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 34:SciSearch(R) Cited Ref Sci 1990-2003/Feb W3

(c) 2003 Inst for Sci Info

*File 34: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 340:CLAIMS(R)/US Patent 1950-03/Feb 20

(c) 2003 IFI/CLAIMS(R)

*File 340: The Claims U.S. Patent databases have been reloaded.

HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.

Set Items Description

--- -----

? s prevent?

S1 1775210 PREVENT?

? s cancer or tumor or malignan? or carcinoma

1166376 CANCER

1274207 TUMOR

483393 MALIGNAN?

722566 CARCINOMA

S2 2588938 CANCER OR TUMOR OR MALIGNAN? OR CARCINOMA

? s s1 and s2

1775210 S1

2588938 S2

S3 145073 S1 AND S2

? s lymphocyte??

S4 678612 LYMPHOCYTE??

? s s3 and s4

145073 S3

678612 S4

S5 8058 S3 AND S4

? s activated or cd(w)3 or cd3 or okt3 or okt(w)3 or interleukin(w)2

Processing

Processing

Processing

658786 ACTIVATED

150106 CD

8814403 3

1190 CD(W)3

54996 CD3

7507 OKT3

1239 OKT

8814403 3

518 OKT(W)3

373138 INTERLEUKIN

10337636 2

108074 INTERLEUKIN(W)2

S6 781977 ACTIVATED OR CD(W)3 OR CD3 OR OKT3 OR OKT(W)3 OR
INTERLEUKIN(W)2

? s s5 and s6

8058 S5

781977 S6

S7 2486 S5 AND S6

? s activated (5n) lymphocyte??

658786 ACTIVATED

678612 LYMPHOCYTE??

S8 21175 ACTIVATED (5N) LYMPHOCYTE??

```

? s s3 and s8
      145073  S3
      21175  S8
      S9      389  S3 AND S8
? s s9 and py<=2001
Processing
Processing
      389  S9
      40185934  PY<=2001
      S10      358  S9 AND PY<=2001
? s five 9w)years
      S11      0  FIVE 9W)YEARS
? s five(w)years
      936994  FIVE
      1404108  YEARS
      S12      29135  FIVE(W)YEARS
? s s10 and s12
      358  S10
      29135  S12
      S13      0  S10 AND S12
? s chemotherap? or surgical or surgery
      344568  CHEMOTHERAP?
      866497  SURGICAL
      1610116  SURGERY
      S14 2247622  CHEMOTHERAP? OR SURGICAL OR SURGERY
? s s10 and s14
      358  S10
      2247622  S14
      S15      31  S10 AND S14
? t s15/3,k,ab/1-31

```

15/3,K,AB/1 (Item 1 from file: 155)
 DIALOG(R) File 155:MEDLINE(R)
 (c) format only 2003 The Dialog Corp. All rts. reserv.

12531652 21395028 PMID: 11504281
 National Oncology Forum: perspectives for the year 2000.
 DeVita V T; Bleickardt E W
 Yale Cancer Center and the Yale University School of Medicine, New Haven,
 Connecticut 06519, USA.
 Cancer journal (Sudbury, Mass.) (United States) Jul-Aug 2001, 7
 Suppl 1 pS2-13, ISSN 1528-9117 Journal Code: 100931981
 Document type: Journal Article; Review; Review, Tutorial
 Languages: ENGLISH
 Main Citation Owner: NLM
 Record type: Completed

Despite advances in treatment, long-term outcome of patients with diffuse large B cell lymphoma (DLBCL) is no better today than reported in 1975. A recent study applying DNA microarray technology revealed that patients whose **cancer** related to patterns of genes expressed in germinal center lymphocytes responded more favorably to **chemotherapy** than patients whose **cancer** related to patterns of genes expressed in **activated lymphocytes**. cDNA and oligonucleotide microarrays are described, and their applications in **cancer** research are reviewed. In addition to DLBCL, microarray technology has been used to study several types of **cancer**. The applications of microarray technology are numerous and include profiling gene expression patterns in order to facilitate diagnosis and predict response to therapy; correlating patterns of gene expression with prognosis; and identifying genes and gene products that are associated with tumorigenic phenotype or with drug resistance, among other applications. Microarray technology has also been used in cell lines to correlate gene expression and **chemotherapy** response. Furthermore, microarray technology may provide a useful tool to examine the development of drug resistance in **cancer** and has recently been used

to study changes in gene expression caused by activated c-Myc in primary human fibroblasts. Tissue microarrays are described. In addition to the amplification of limited tissue resources, tissue microarrays have the advantages of limiting the variability associated with tissue processing and limiting the necessary amount of reagent. Tissue microarrays have been used to determine the frequencies of amplification of 3 major breast **cancer** genes and identify overexpression of ERBB2 mRNA; assess and compare gene amplification in benign prostatic hyperplasia, primary prostate **carcinoma**, recurrent prostate tumors, and metastatic tumors; compare aggressiveness of prostate **carcinoma** in 2 patient populations; and study gene amplification across various **tumor** types. Furthermore, DNA microarray and tissue microarray techniques can be combined to provide convergent evidence of findings and to examine different aspects of gene expression. DNA array technology may also be used to identify critical molecular targets or to identify the critical rate-limiting step in a cascade of genes under the influence of a mutated gene. The historical progression of goals of the National **Cancer** Institute is reviewed, as well as the economic impact of reduction in **cancer**-associated mortality. Future efforts should continue the investment in basic research and more effectively integrate it with clinical trials and with approaches to **prevention** and treatment.

Jul-Aug 2001,

... than reported in 1975. A recent study applying DNA microarray technology revealed that patients whose **cancer** related to patterns of genes expressed in germinal center lymphocytes responded more favorably to **chemotherapy** than patients whose **cancer** related to patterns of genes expressed in **activated lymphocytes**. cDNA and oligonucleotide microarrays are described, and their applications in **cancer** research are reviewed. In addition to DLBCL, microarray technology has been used to study several types of **cancer**. The applications of microarray technology are numerous and include profiling gene expression patterns in order...

... other applications. Microarray technology has also been used in cell lines to correlate gene expression and **chemotherapy** response. Furthermore, microarray technology may provide a useful tool to examine the development of drug resistance in **cancer** and has recently been used to study changes in gene expression caused by activated c...

... Tissue microarrays have been used to determine the frequencies of amplification of 3 major breast **cancer** genes and identify overexpression of ERBB2 mRNA; assess and compare gene amplification in benign prostatic hyperplasia, primary prostate **carcinoma**, recurrent prostate tumors, and metastatic tumors; compare aggressiveness of prostate **carcinoma** in 2 patient populations; and study gene amplification across various **tumor** types. Furthermore, DNA microarray and tissue microarray techniques can be combined to provide convergent evidence...

... under the influence of a mutated gene. The historical progression of goals of the National **Cancer** Institute is reviewed, as well as the economic impact of reduction in **cancer**-associated mortality. Future efforts should continue the investment in basic research and more effectively integrate it with clinical trials and with approaches to **prevention** and treatment.

15/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11331993 21385065 PMID: 11493326
Hepatocellular **carcinoma**: an overview.
Anthony P P

Department of Histopathology, Royal Devon & Exeter Healthcare NHS Trust,
Wonford, Exeter EX2 5AD, UK.

Histopathology (England) Aug 2001, 39 (2) p109-18, ISSN
0309-0167 Journal Code: 7704136

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Hepatocellular **carcinoma** remains widely prevalent in tropical Africa and south-east Asia and is largely related to chronic hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour incidence cannot be expected for decades to come yet, even in those countries in which the necessary resources exist, as millions of adults remain chronically infected. Meanwhile, the incidence is rising in Japan, Mediterranean countries of Europe, Middle East and North Africa and in the USA, largely due to chronic hepatitis C virus (HCV) infection introduced by the indiscriminate use of unscreened blood and blood products in the recent past. Much has been learned from molecular biological studies on hepatocarcinogenesis incriminating the HBX gene of HBV, the core protein of HCV and a unique guanine to thymine transversion at codon 249 has been observed in cases due to aflatoxin exposure. The subject of precancerous lesions, notably adenomatous/dysplastic nodules and large-cell/small-cell change continues to be a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases.

Hepatocellular **carcinoma**: an overview.

Aug 2001,

Hepatocellular **carcinoma** remains widely prevalent in tropical Africa and south-east Asia and is largely related to chronic hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour...

... a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases.

Descriptors: **Carcinoma**, Hepatocellular--pathology--PA; *Liver Neoplasms--pathology--PA; **Carcinoma**, Hepatocellular--metabolism--ME; **Carcinoma**, Hepatocellular--virology--VI; Hepacivirus--genetics--GE; Hepatitis B--pathology--PA; Hepatitis B--virology--VI; Hepatitis...

...pathology--PA; Hepatitis C--virology--VI; Immunohistochemistry; Liver Neoplasms--metabolism--ME; Liver Neoplasms--virology--VI; **Tumor** Markers, Biological--analysis--AN

Chemical Name: **Tumor** Markers, Biological

15/3,K,AB/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

10898644 20475764 PMID: 11022927

Adoptive immunotherapy to lower postsurgical recurrence rates of

hepatocellular **carcinoma**: a randomised trial.

Takayama T; Sekine T; Makuuchi M; Yamasaki S; Kosuge T; Yamamoto J; Shimada K; Sakamoto M; Hirohashi S; Ohashi Y; Kakizoe T

Department of Surgery, National Cancer Research Institute, University of Tokyo, Japan. takayamat-2su@h.u-tokyo.ac.jp

Lancet (ENGLAND) Sep 2 2000, 356 (9232) p802-7, ISSN 0140-6736 Journal Code: 2985213R

Comment in Lancet. 2000 Sep 2;356(9232) 784-5; Comment in PMID 11022921; Erratum in Lancet 2000 Nov 11;356(9242):1690

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: Postsurgical recurrence of hepatocellular **carcinoma** (HCC) is frequent and fatal. Adoptive immunotherapy is active against HCC. We assessed whether postoperative immunotherapy could lower the frequency of recurrence. METHODS: Between 1992 and 1995, we did a randomised trial in which 150 patients who had undergone curative resection for HCC were assigned adoptive immunotherapy (n=76) or no adjuvant treatment (n=74). Autologous **lymphocytes activated** vitro with recombinant interleukin-2 and antibody to CD3 were infused five times during the first 6 months. Primary endpoints were time to first recurrence and recurrence-free survival and analyses were by intention to treat. FINDINGS: 76 patients received 370 (97%) of 380 scheduled lymphocyte infusions (mean cell number per patient 7.1×10^{10} [SD 2.1]; CD3 and HLA-DR cells 78% [16]), and none had grade 3 or 4 adverse events. After a median follow-up of 4.4 years (range 0.2-6.7), adoptive immunotherapy decreased the frequency of recurrence by 18% compared with controls (45 [59%] vs 57 [77%]) [corrected] patients. Time to first recurrence in the immunotherapy group was significantly longer than that in the control group (48% [37-59] vs 33% [22-43] at 3 years, 38% [22-54] vs 22% [11-34] at 5 years; p=0.008). The immunotherapy group had significantly longer recurrence-free survival (p=0.01) and disease-specific survival (p=0.04) than the control group. Overall survival did not differ significantly between groups (p=0.09). INTERPRETATION: Adoptive immunotherapy is a safe, feasible treatment that can lower recurrence and improve recurrence-free outcomes after **surgery** for HCC.

Adoptive immunotherapy to lower postsurgical recurrence rates of hepatocellular **carcinoma**: a randomised trial.

Sep 2 2000,

BACKGROUND: Postsurgical recurrence of hepatocellular **carcinoma** (HCC) is frequent and fatal. Adoptive immunotherapy is active against HCC. We assessed whether postoperative...

... for HCC were assigned adoptive immunotherapy (n=76) or no adjuvant treatment (n=74). Autologous **lymphocytes activated** vitro with recombinant interleukin-2 and antibody to CD3 were infused five times during the...

... is a safe, feasible treatment that can lower recurrence and improve recurrence-free outcomes after **surgery** for HCC.

Descriptors: **Carcinoma**, Hepatocellular--therapy--TH; *Immunotherapy --methods--MT; *Liver Neoplasms--therapy--TH; Adult; Aged; Aged, 80 and over; **Carcinoma**, Hepatocellular--**surgery**--SU; Disease-Free Survival; Hepatectomy; Immunotherapy--adverse effects--AE; Interleukin-2 --administration and dosage--AD; Interleukin-2--therapeutic use--TU; Liver Neoplasms--**surgery**--SU; Middle Age; Neoplasm Recurrence, Local--**prevention** and control--PC; Postoperative Period

(c) format only 2003 The Dialog Corp. All rts. reserv.

10699248 20231477 PMID: 10767797

Hepatic cryoablation, but not radiofrequency ablation, results in lung inflammation.

Chapman W C; Debelak J P; Wright Pinson C; Washington M K; Atkinson J B; Venkatakrishnan A; Blackwell T S; Christman J W

Division of Hepatobiliary Surgery and Liver Transplantation, Vanderbilt University Medical Center, Nashville, TN, USA. will.chapman@surgery.mc.vanderbilt.edu

Annals of surgery (UNITED STATES) May 2000, 231 (5) p752-61,

ISSN 0003-4932 Journal Code: 0372354

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

OBJECTIVE: To compare the effects of 35% hepatic cryoablation with a similar degree of radiofrequency ablation (RFA) on lung inflammation, nuclear factor kappaB (NF-kappaB) activation, and production of NF-kappaB dependent cytokines. **SUMMARY BACKGROUND DATA:** Multisystem injury, including acute lung injury, is a severe complication associated with hepatic cryoablation of 30% to 35% or more of liver parenchyma, but this complication has not been reported with RFA. **METHODS:** Sprague-Dawley rats underwent 35% hepatic cryoablation or RFA and were killed at 1, 2, and 6 hours. Liver and lung tissue were freeze-clamped for measurement of NF-kappaB activation, which was detected by electrophoretic mobility shift assay. Serum concentrations of tumor necrosis factor alpha and macrophage inflammatory protein 2 were measured by enzyme-linked immunosorbent assay. Histologic studies of pulmonary tissue and electron microscopy of ablated liver tissue were compared among treatment groups. **RESULTS:** Histologic lung sections after cryoablation showed multiple foci of perivenular inflammation, with **activated lymphocytes**, foamy macrophages, and neutrophils. In animals undergoing RFA, inflammatory foci were not present. NF-kappaB activation was detected at 1 hour in both liver and lung tissue samples of animals undergoing cryoablation but not after RFA, and serum cytokine levels were significantly elevated in cryoablation versus RFA animals. Electron microscopy of cryoablation-treated liver tissue demonstrated disruption of the hepatocyte plasma membrane with extension of intact hepatocyte organelles into the space of Disse; RFA-treated liver tissue demonstrated coagulative destruction of hepatocyte organelles within an intact plasma membrane. To determine the stimulus for systemic inflammation, rats treated with cryoablation had either immediate resection of the ablated segment or delayed resection after a 15-minute thawing interval. Immediate resection of the cryoablated liver tissue **prevented** NF-kappaB activation and lung injury; however, pulmonary inflammatory changes were present when as little as a 15-minute thaw interval preceded hepatic resection. **CONCLUSIONS:** Hepatic cryoablation, but not RFA, induces NF-kappaB activation in the nonablated liver and lung and is associated with acute lung injury. Lung inflammation is associated with the thawing phase of cryoablation and may be related to soluble mediator(s) released from the cryoablated tissue. These findings correlate the clinical observation of an increased incidence of multisystem injury, including adult respiratory distress syndrome (ARDS), after cryoablation but not RFA.

May 2000,

... of NF-kappaB activation, which was detected by electrophoretic mobility shift assay. Serum concentrations of tumor necrosis factor alpha and macrophage inflammatory protein 2 were measured by enzyme-linked immunosorbent assay...

... treatment groups. **RESULTS:** Histologic lung sections after cryoablation showed multiple foci of perivenular inflammation, with **activated lymphocytes**, foamy macrophages, and neutrophils. In animals undergoing RFA, inflammatory foci were not present. NF-kappaB...

... delayed resection after a 15-minute thawing interval. Immediate resection of the cryoablated liver tissue **prevented** NF-kappaB activation and lung injury; however, pulmonary inflammatory changes were present when as little...

Descriptors: Catheter Ablation; *Cryosurgery; *Liver--**surgery**--SU; *Sepsis Syndrome--etiology--ET...; PA; Microscopy, Electron; Monokines--blood--BL; NF-kappa B--metabolism--ME; Rats; Rats, Sprague-Dawley; **Tumor** Necrosis Factor--analysis--AN

Chemical Name: Chemotactic Factors; Monokines; NF-kappa B; **Tumor** Necrosis Factor; macrophage inflammatory protein 2

15/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10364776 99362923 PMID: 10432288

Bcl-2-mediated drug resistance: inhibition of apoptosis by blocking nuclear factor of **activated T lymphocytes** (NFAT)-induced Fas ligand transcription.

Srivastava R K; Sasaki C Y; Hardwick J M; Longo D L
Laboratory of Immunology, National Institute on Aging, National Institutes of Health, Baltimore, Maryland 21224-6825, USA.
rakeshs@vax.grc.nia.nih.gov

Journal of experimental medicine (UNITED STATES) Jul 19 1999,
190 (2) p253-65, ISSN 0022-1007 Journal Code: 2985109R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Bcl-2 inhibits apoptosis induced by a variety of stimuli, including **chemotherapy** drugs and glucocorticoids. It is generally accepted that Bcl-2 exerts its antiapoptotic effects mainly by dimerizing with proapoptotic members of the Bcl-2 family such as Bax and Bad. However, the mechanism of the antiapoptotic effects is unclear. Paclitaxel and other drugs that disturb microtubule dynamics kill cells in a Fas/Fas ligand (FasL)-dependent manner; antibody to FasL inhibits paclitaxel-induced apoptosis. We have found that Bcl-2 overexpression leads to the **prevention** of **chemotherapy** (paclitaxel)-induced expression of FasL and blocks paclitaxel-induced apoptosis. The mechanism of this effect is that Bcl-2 **prevents** the nuclear translocation of NFAT (nuclear factor of **activated T lymphocytes**, a transcription factor **activated** by microtubule damage) by binding and sequestering calcineurin, a calcium-dependent phosphatase that must dephosphorylate NFAT to move to the nucleus. Without NFAT nuclear translocation, the FasL gene is not transcribed. Thus, it appears that paclitaxel and other drugs that disturb microtubule function kill cells at least in part through the induction of FasL. Furthermore, Bcl-2 antagonizes drug-induced apoptosis by inhibiting calcineurin activation, blocking NFAT nuclear translocation, and **preventing** FasL expression. The effects of Bcl-2 can be overcome, at least partially, through phosphorylation of Bcl-2. Phosphorylated Bcl-2 cannot bind calcineurin, and NFAT activation, FasL expression, and apoptosis can occur after Bcl-2 phosphorylation.

Bcl-2-mediated drug resistance: inhibition of apoptosis by blocking nuclear factor of **activated T lymphocytes** (NFAT)-induced Fas ligand transcription.

Jul 19 1999,

Bcl-2 inhibits apoptosis induced by a variety of stimuli, including **chemotherapy** drugs and glucocorticoids. It is generally accepted that Bcl-2 exerts its antiapoptotic effects mainly...

... FasL inhibits paclitaxel-induced apoptosis. We have found that Bcl-2

overexpression leads to the **prevention** of **chemotherapy** (paclitaxel)-induced expression of FasL and blocks paclitaxel-induced apoptosis. The mechanism of this effect is that Bcl-2 **prevents** the nuclear translocation of NFAT (nuclear factor of **activated** T **lymphocytes**, a transcription factor **activated** by microtubule damage) by binding and sequestering calcineurin, a calcium-dependent phosphatase that must dephosphorylate...

... Bcl-2 antagonizes drug-induced apoptosis by inhibiting calcineurin activation, blocking NFAT nuclear translocation, and **preventing** FasL expression. The effects of Bcl-2 can be overcome, at least partially, through phosphorylation...

...; Oncogene Proteins c-bcl-2--metabolism--ME; Signal Transduction; T-Lymphocytes--cytology--CY; Transcription, Genetic; **Tumor** Cells, Cultured

15/3,K,AB/6 (Item 6 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10333978 99323381 PMID: 10397252
Fas-FasL-mediated CD4+ T-cell apoptosis following stem cell transplantation.

Singh R K; Varney M L; Buyukberber S; Ino K; Ageitos A G; Reed E; Tarantolo S; Talmadge J E

Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha 68198-5660, USA.

Cancer research (UNITED STATES) Jul 1 1999, 59 (13) p3107-11,
ISSN 0008-5472 Journal Code: 2984705R

Contract/Grant No.: R01-CA61593; CA; NCI; R29-CA72781; CA; NCI

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We report the preferential expression of Fas on CD4+ T cells and Fas ligand (FasL) on monocytes and their potential role in the selective loss of CD4+ T cells in breast **cancer** patients undergoing high-dose **chemotherapy** and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4+ T cells (28-51%) is observed during the first 100 days after PSCT concomitant with a significant increase in monocyte frequency and FasL expression (11.6-23%) on monocytes. The preferential expression of Fas on CD4+ T cells (73-92%) in the peripheral blood (PB) of these patients is associated with a significantly higher frequency of CD4+ T-cell apoptosis compared with CD8+ T cells (28-47%) and CD4+ T cells (46 +/- 5.7%) in normal PB. These data suggest that "primed" Fas+ CD4+ **lymphocytes** interact with **activated** monocytes that express FasL, resulting in apoptosis, leading to deletion of CD4+ T cells, an inversion in the CD4:CD8 T-cell ratio, and immune dysfunction. The **prevention** of CD4+ T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem cell products, blockade of Fas-FasL interactions, or cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

Jul 1 1999,

... monocytes and their potential role in the selective loss of CD4+ T cells in breast **cancer** patients undergoing high-dose **chemotherapy** and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4+ T cells...

... T cells (46 +/- 5.7%) in normal PB. These data suggest that "primed" Fas+ CD4+ **lymphocytes** interact with **activated** monocytes that express FasL, resulting in apoptosis, leading to deletion of CD4+ T cells,

an inversion in the CD4:CD8 T-cell ratio, and immune dysfunction. The **prevention** of CD4+ T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem...

... cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

Descriptors: Antigens, CD95--physiology--PH; *Antineoplastic Combined **Chemotherapy** Protocols--therapeutic use--TU; *Apoptosis; *Breast Neoplasms--therapy--TH; *CD4-Positive T-Lymphocytes--immunology--IM...

Chemical Name: Antigens, CD95; Antineoplastic Combined **Chemotherapy** Protocols; FasL protein; Membrane Glycoproteins

15/3,K,AB/7 (Item 7 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

09527942 97435374 PMID: 9290119

Immunomodulatory effect of beta-carotene on T lymphocyte subsets in patients with resected colonic polyps and **cancer**.

Kazi N; Radvany R; Oldham T; Keshavarzian A; Frommel T O; Libertin C; Mobarhan S

Department of Medicine, Loyola University Medical Center, Maywood, IL 60153, USA.

Nutrition and cancer (UNITED STATES) 1997, 28 (2) p140-5,
ISSN 0163-5581 Journal Code: 7905040

Contract/Grant No.: CA-53799; CA; NCI

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Results from a number of studies suggest that beta-carotene-containing foods **prevent** the initiation or progression of various cancers. One possible mechanism for this effect could be enhancement of the immune response. The aim of this study was to determine whether beta-carotene modulates T lymphocyte subsets in patients affected with colonic polyps or cancerous lesions. Patients with previous adenomatous colonic polyps (n = 18) or colon cancers (n = 19) were randomized to receive placebo or beta-carotene (30 mg/day) for three months. Percentages of T lymphocyte subsets were determined using flow cytometry in blood samples collected before randomization and at three months. T lymphocyte subsets of 14 normal control subjects were also determined for comparison. Initially, there was no difference in total leukocyte counts, percentage of lymphocytes, and various subsets of lymphocytes among the three groups, although in **cancer** patients there was a lower percentage of CD4 and interleukin-2 (IL-2) receptor-positive (IL-2R+) cells than in patients with polyps and in controls. After supplementation with beta-carotene, a significant increase in IL-2R+ T lymphocytes (from 12.7 +/- 3.0% to 26.0 +/- 1.9%) and CD4+ lymphocytes (from 40.9 +/- 3.1% to 45.6 +/- 3.2%) was seen only in the **cancer** patients. These percentages remained unchanged in patients with adenomatous polyps receiving placebo or beta-carotene. We concluded that beta-carotene increased the number of IL-2R+ T lymphocytes and CD4+ lymphocytes, which in turn may produce IL-2 only in patients with **cancer** who may already have some deficiency in their immune system. This increase in **activated T lymphocytes** may mediate cytotoxic reactions to **cancer** cells via cytokine production.

... effect of beta-carotene on T lymphocyte subsets in patients with resected colonic polyps and **cancer**.

1997,

Results from a number of studies suggest that beta-carotene-containing foods **prevent** the initiation or progression of various cancers. One

possible mechanism for this effect could be...

... counts, percentage of lymphocytes, and various subsets of lymphocytes among the three groups, although in **cancer** patients there was a lower percentage of CD4 and interleukin-2 (IL-2) receptor-positive...

...from 40.9 +/- 3.1% to 45.6 +/- 3.2%) was seen only in the **cancer** patients. These percentages remained unchanged in patients with adenomatous polyps receiving placebo or beta-carotene...

...lymphocytes and CD4+ lymphocytes, which in turn may produce IL-2 only in patients with **cancer** who may already have some deficiency in their immune system. This increase in **activated T lymphocytes** may mediate cytotoxic reactions to **cancer** cells via cytokine production.

; Adult; Cohort Studies; Colonic Neoplasms--**surgery**--SU; Colonic Polyps--**surgery**--SU; Flow Cytometry; Middle Age; Reference Values; T-Lymphocyte Subsets--immunology--IM; Time Factors; Tretinoin...

15/3,K,AB/8 (Item 8 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

08987963 96366593 PMID: 8770770

Adoptive transfer of bryostatin-**activated tumor**-sensitized **lymphocytes** prevents or destroys **tumor** metastases without expansion in vitro.

Fleming M D; Bear H D; Lipshy K; Kostuchenko P J; Portocarero D; McFadden A W; Barrett S K

Department of Surgery, Medical College of Virginia, Virginia Commonwealth University, Richmond, USA.

Journal of immunotherapy with emphasis on tumor immunology : official journal of the Society for Biological Therapy (UNITED STATES) Oct 1995, 18 (3) p147-55, ISSN 1067-5582 Journal Code: 9418950

Contract/Grant No.: CA48075; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Because the requirement for long-term cell culture can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor**-sensitized T cells activated briefly with bryostatin 1 and ionomycin (B/I) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas were harvested and treated for 18 h with B/I. These cells were then washed and transferred immediately to naive C57B1/6 mice. In some experiments, these mice were irradiated (500 rads) before adoptive transfer and were given interleukin-2 (IL-2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated lymphocytes**. Recipient mice were challenged with sarcoma cells (4 x 10⁵) i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10⁶ B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous IL-2 or host irradiation. Using Thy-1 congenic donors, it was shown that B/I-activated T cells expanded in recipients when IL-2 was also given, and these cells were a prominent component (15% of total cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-"pulsed" cells with cyclophosphamide (CYP) and IL-2 to treat mice with established (3-day) metastases resulted in significant reduction in pulmonary nodules, with complete regression in many of the treated mice, which was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor**

-sensitized, B/I-activated DLN cells confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor cells activated with B/I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

Adoptive transfer of bryostatin-**activated tumor**-sensitized **lymphocytes** prevents or destroys **tumor** metastases without expansion in vitro.

Oct 1995,

... can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor**-sensitized T cells activated briefly with bryostatin 1 and ionomycin (B/I) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas...

...2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated lymphocytes**. Recipient mice were challenged with sarcoma cells (4 x 10(5) i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10(6) B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous...

...cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-"pulsed" cells with cyclophosphamide (CYP) and IL-2 to treat...

... was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor**-sensitized, B/I-activated DLN cells confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor ...

... I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

15/3,K,AB/9 (Item 9 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

08153392 94290375 PMID: 7912603

Reconstitution of lymphocyte subsets after peripheral blood stem cell transplantation: two-color flow cytometric analysis.

Ashihara E; Shimazaki C; Yamagata N; Hirata T; Okawa K; Oku N; Goto H; Inaba T; Fujita N; Nakagawa M

Second Department of Medicine, Kyoto Prefectural University of Medicine, Japan.

Bone marrow transplantation (ENGLAND) Apr 1994, 13 (4) p377-81
, ISSN 0268-3369 Journal Code: 8702459

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The reconstitution of lymphocyte subsets after high-dose **chemotherapy** followed by peripheral blood stem cell transplantation (PBSCT) was studied using two-color flow cytometry in 14 patients with acute leukemia (four AML and two ALL) and **malignant** lymphoma (six NHL

and two HD). The CD3+HLA-DR+ **lymphocytes (activated T cells)** and CD8+ **lymphocytes** increased markedly by 4 weeks after PBSCT. Most of the increased CD8+ lymphocytes were CD11b-, S6F1+ cells and CD8+CD11b+ cells remained low throughout the follow-up period. The CD4+ lymphocytes remained below the normal range up to 34 weeks after PBSCT. The ratio of CD4+ to CD8+ lymphocytes (CD4/CD8 ratio) transiently increased and then decreased below 1.0 at 2 weeks after PBSCT. The CD19+ lymphocytes and the CD3-CD16+CD56+ lymphocytes returned to normal levels in the early period. The CD4+CD45RA+ lymphocytes (suppressor-inducer) decreased to below the normal range, while the CD4+CD45RO+ lymphocytes (helper-inducer) increased more rapidly than the CD4+CD45RA+ lymphocytes. This study shows that an immunosuppressed state exists after PBSCT as is seen after bone marrow transplantation (BMT) and that B cell reconstitution is more rapid in PBSCT than in BMT.

Apr 1994,

The reconstitution of lymphocyte subsets after high-dose chemotherapy followed by peripheral blood stem cell transplantation (PBSCT) was studied using two-color flow cytometry in 14 patients with acute leukemia (four AML and two ALL) and **malignant lymphoma (six NHL and two HD)**. The CD3+HLA-DR+ **lymphocytes (activated T cells)** and CD8+ **lymphocytes** increased markedly by 4 weeks after PBSCT. Most of the increased CD8+ lymphocytes were CD11b...

...; Therapy; Etoposide--adverse effects--AE; Etoposide--therapeutic use --TU; Graft Survival; Graft vs Host Disease--**prevention** and control --PC; Leukemia, Lymphocytic, Acute, L2--drug therapy--DT; Leukemia, Lymphocytic, Acute, L2--therapy...

15/3,K,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

08104556 94255178 PMID: 8196915

Immunochemotherapy in B-16-melanoma-cell-transplanted mice with combinations of interleukin-2, cyclophosphamide, and PSK.

Ueno Y; Kohgo Y; Sakamaki S; Itoh Y; Takahashi M; Hirayama Y; Niitsu Y
Department of Internal Medicine (Section 4), Sapporo Medical University School of Medicine, Japan.

Oncology (SWITZERLAND) May-Jun 1994, 51 (3) p296-302, ISSN 0030-2414 Journal Code: 0135054

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The effect of combination immunochemotherapy using interleukin-2 (IL-2), PSK and cyclophosphamide (CY) was evaluated in a pulmonary metastasis model in BDF1 mice. B-16 melanoma cells were inoculated into a hind limb. On day 3 after inoculation, 20 mg/kg of CY was administered intraperitoneally, and IL-2 (3.75 x 10⁴ BRM units/head) was injected into the tail vein on days 7, 8 and 9. PSK (1,000 mg/kg) was administered orally every day from day 1 to day 10 using a stomach tube. This treatment cycle was repeated three times. Using this combination therapy, the cytotoxicity of lymphokine-**activated killer cells** and **tumor-infiltrating lymphocytes** was enhanced. Pulmonary metastasis was remarkably suppressed and a prolongation of survival was obtained compared with the nontreated group and an IL-2+CY group. The effect was augmented by repeating the therapy protocol. By analyzing the killer activity and surface markers of **tumor-infiltrating lymphocytes**, it was recognized that increased numbers of Lyt-2-positive T cells with augmented cytotoxicity were obtained. This treatment modality should have clinical significance.

May-Jun 1994,

... This treatment cycle was repeated three times. Using this combination

therapy, the cytotoxicity of lymphokine-**activated** killer cells and **tumor-infiltrating lymphocytes** was enhanced. Pulmonary metastasis was remarkably suppressed and a prolongation of survival was obtained compared...

... augmented by repeating the therapy protocol. By analyzing the killer activity and surface markers of **tumor-infiltrating lymphocytes**, it was recognized that increased numbers of Lyt-2-positive T cells with...

Descriptors: Antineoplastic Combined **Chemotherapy** Protocols --therapeutic use--TU; *Immunotherapy; *Melanoma, Experimental--therapy--TH ...; IM; Interleukin-2--administration and dosage--AD; Killer Cells, Lymphokine-Activated--immunology--IM; Lung Neoplasms--**prevention** and control--PC; Lung Neoplasms--secondary--SC; Lymphocytes, **Tumor** -Infiltrating--immunology--IM; Melanoma, Experimental--drug therapy--DT; Melanoma, Experimental--immunology--IM; Mice; Mice, Inbred...

Chemical Name: Antibiotics, Antineoplastic; Antigens, Neoplasm; Antigens, Surface; Antineoplastic Combined **Chemotherapy** Protocols; Biological Response Modifiers; Interleukin-2; Proteoglycans; Cyclophosphamide; PS-K

15/3,K,AB/11 (Item 11 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

06657417 90358528 PMID: 1697153

Bases on timing of combined modality of **chemotherapy** and immunotherapy]

Ogura T

Third Dept. of Internal Medicine, School of Medicine, Tokushima University.

Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Aug 1990, 17

(8 Pt 1) p1414-20, ISSN 0385-0684 Journal Code: 7810034

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: Completed

Chemoimmunotherapy with anticancer drugs and immunoregulatory drugs and cytokines is a logical combination of 2 forms of therapy that have different mechanisms of action and no overlapping toxicity. Generally, anticancer drugs show rapidly the strong suppressive effect on **tumor** growth but also on host hemato-immunological functions. On the other hand, immunotherapy demonstrate the potential of restoring the hemato-immunological dysfunction of **chemotherapy** as well as the gradual antitumor effect through activating host defense mechanisms against **cancer**, indicating that these therapeutic modalities are complementary. On these biological rationale of chemoimmunotherapy mentioned above, we have demonstrated that immunostimulant, Nocardia-CWS is capable of producing tumoricidal macrophages being different from anticancer drugs in cytotoxic mechanism against **cancer**, and also that macrophage tumoricidal activity is significantly suppressed by exposure to anticancer drug, mitomycin C. Another beneficial activity of immunostimulant showed in our previous studies is a capability of production of colony stimulating activities. In a cooperative study with lung **cancer** patients it has been shown that recovery of leucopenia after **chemotherapy** is accelerated by administration of immunostimulant, MDP-Lys. Recently, immunomodulatory lymphokine, IL-2, has been clinically used for induction of **activated** killer **lymphocytes** (LAK cells) with tumoricidal activity. According to our studies, however, anticancer drug, when administered to **cancer** patients or added directly to culture of lymphocytes with IL-2 for LAK induction, shows significant suppressive effect on LAK induction. Considering these experimental and clinical studies, it can be concluded that immunotherapy, when employed as adjuvant after **chemotherapy**,

play the important roles not only in eradication of **tumor** cells being escaped from **chemotherapy** but also in **prevention** of infections complication by activating host defense mechanisms common to **cancer** and infection.

Bases on timing of combined modality of **chemotherapy** and immunotherapy]

Aug 1990,

... action and no overlapping toxicity. Generally, anticancer drugs show rapidly the strong suppressive effect on **tumor** growth but also on host hemato-immunological functions. On the other hand, immunotherapy demonstrate the potential of restoring the hemato-immunological dysfunction of **chemotherapy** as well as the gradual antitumor effect through activating host defense mechanisms against **cancer**, indicating that these therapeutic modalities are complementary. On these biological rationale of chemoimmunotherapy mentioned above...

... is capable of producing tumoricidal macrophages being different from anticancer drugs in cytotoxic mechanism against **cancer**, and also that macrophage tumoricidal activity is significantly suppressed by exposure to anticancer drug, mitomycin...

... is a capability of production of colony stimulating activities. In a cooperative study with lung **cancer** patients it has been shown that recovery of leucopenia after **chemotherapy** is accelerated by administration of immunostimulant, MDP-Lys. Recently, immunomodulatory lymphokine, IL-2, has been clinically used for induction of **activated** killer **lymphocytes** (LAK cells) with tumoricidal activity. According to our studies, however, anticancer drug, when administered to **cancer** patients or added directly to culture of lymphocytes with IL-2 for LAK induction, shows...

... experimental and clinical studies, it can be concluded that immunotherapy, when employed as adjuvant after **chemotherapy**, play the important roles not only in eradication of **tumor** cells being escaped from **chemotherapy** but also in **prevention** of infections complication by activating host defense mechanisms common to **cancer** and infection.

15/3,K,AB/12 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13230976 BIOSIS NO.: 200100438125
Hepatocellular **carcinoma**: An overview.
AUTHOR: Anthony P P(a)
AUTHOR ADDRESS: (a)Department of Histopathology, Royal Devon and Exeter
Hospital, Wonford, Exeter, EX2 5AD**UK
JOURNAL: Histopathology (Oxford) 39 (2):p109-118 August, 2001
MEDIUM: print
ISSN: 0309-0167
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Hepatocellular **carcinoma** remains widely prevalent in tropical Africa and south-east Asia and is largely related to chronic hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour incidence cannot be expected for decades to come yet, even in those countries in which the necessary resources exist, as millions of adults remain chronically infected. Meanwhile, the incidence is rising in

Japan, Mediterranean countries of Europe, Middle East and North Africa and in the USA, largely due to chronic hepatitis C virus (HCV) infection introduced by the indiscriminate use of unscreened blood and blood products in the recent past. Much has been learned from molecular biological studies on hepatocarcinogenesis incriminating the HBX gene of HBV, the core protein of HCV and a unique guanine to thymine transversion at codon 249 has been observed in cases due to aflatoxin exposure. The subject of precancerous lesions, notably adenomatous/dysplastic nodules and large-cell/small-cell change continues to be a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases.

2001

Hepatocellular **carcinoma**: An overview.

2001

ABSTRACT: Hepatocellular **carcinoma** remains widely prevalent in tropical Africa and south-east Asia and is largely related to chronic hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour...

...a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases.

DESCRIPTORS:

...MAJOR CONCEPTS: **Tumor** Biology

...DISEASES: hepatocellular **carcinoma**--

MISCELLANEOUS TERMS: ...**tumor** regression

ALTERNATE INDEXING: ... **Carcinoma**, Hepatocellular (MeSH)

15/3,K,AB/13 (Item 2 from file: 55)

DIALOG(R) File 55:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

12056425 BIOSIS NO.: 199900336944

Fas-FasL-mediated CD4+ T-cell apoptosis following stem cell transplantation.

AUTHOR: Singh Rakesh K; Varney Michelle L; Buyukberber Suleyman; Ino Kazuhiko; Ageitos Ana G; Reed Elizabeth; Tarantolo Stefano; Talmadge James E(a)

AUTHOR ADDRESS: (a)Department of Pathology and Microbiology, University of Nebraska Medical Center, 985660 Nebraska**USA

JOURNAL: Cancer Research 59 (13):p3107-3111 July 1, 1999

ISSN: 0008-5472

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: We report the preferential expression of Fas on CD4+ T cells and Fas ligand (FasL) on monocytes and their potential role in the selective

loss of CD4+ T cells in breast **cancer** patients undergoing high-dose **chemotherapy** and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4+ T cells (28-51%) is observed during the first 100 days after PSCT concomitant with a significant increase in monocyte frequency and FasL expression (11.6-23%) on monocytes. The preferential expression of Fas on CD4+ T cells (73-92%) in the peripheral blood (PB) of these patients is associated with a significantly higher frequency of CD4+ T-cell apoptosis compared with CD8+ T cells (28-47%) and CD4+ T cells (46 +/- 5.7%) in normal PB. These data suggest that "primed" Fas+ CD4+ **lymphocytes** interact with **activated** monocytes that express FasL, resulting in apoptosis, leading to deletion of CD4+ T cells, an inversion in the CD4:CD8 T-cell ratio, and immune dysfunction. The **prevention** of CD4+ T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem cell products, blockade of Fas-FasL interactions, or cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

1999

1999

...ABSTRACT: monocytes and their potential role in the selective loss of CD4+ T cells in breast **cancer** patients undergoing high-dose **chemotherapy** and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4+ T cells...
...T cells (46 +/- 5.7%) in normal PB. These data suggest that "primed" Fas+ CD4+ **lymphocytes** interact with **activated** monocytes that express FasL, resulting in apoptosis, leading to deletion of CD4+ T cells, an inversion in the CD4:CD8 T-cell ratio, and immune dysfunction. The **prevention** of CD4+ T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem...
...cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

DESCRIPTORS:

DISEASES: breast **cancer**--...

...adjuvant immunotherapy, high-dose **chemotherapy**, neoplastic disease
, reproductive system disease/female

15/3,K,AB/14 (Item 3 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

2/28

11356861 BIOSIS NO.: 199800138193
Homing of polyclonally activated syngeneic T cells at tumour site and their efficacy in post operative immunotherapy of **malignancy** in mouse.
AUTHOR: Chakravarty Ashim K; Jha Shubra
AUTHOR ADDRESS: Immunol. Cell Biol. Lab., Centre Life Sci., Univ. North Bengal, Siliguri 734 430**India
JOURNAL: Current Science (Bangalore) 73 (2):p201-203 July 25, 1997
ISSN: 0011-3891
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: 3H-Thymidine labelled and polyclonally **activated** syngeneic **lymphocytes** injected intravenously have been found to home preferentially at the fibrosarcoma site in mice from 12 h after adoptive transfer. The highest counts from infiltrating radiolabelled cells were obtained at 24 h at the centre of the tumour. Considering this value as

maximum, all other values are expressed relative to this number. At 12 h lymphocyte infiltration at the periphery of the tumour mass was about 75%, followed by about 40% infiltration in the liver. After 24 h the central region of tumour mass showed the highest infiltration of radioactively labelled lymphocytes, whereas in liver it remained 50%. There was decline in homing of the **activated lymphocytes** after 48 h of adoptive transfer. These tumour site seeking **activated lymphocytes** are likely to recognize the residual **malignant** cells after **surgical** removal of solid tumour, so these cells were adoptively transferred in conjunction with **surgery**. It has been observed in such experiments, the reappearance of tumour was **prevented** in 67% of mice and the survival of the hosts increased.

1997

...activated syngeneic T cells at tumour site and their efficacy in post operative immunotherapy of **malignancy** in mouse.

1997

ABSTRACT: 3H-Thymidine labelled and polyclonally **activated** syngeneic **lymphocytes** injected intravenously have been found to home preferentially at the fibrosarcoma site in mice from...

...labelled lymphocytes, whereas in liver it remained 50%. There was decline in homing of the **activated lymphocytes** after 48 h of adoptive transfer. These tumour site seeking **activated lymphocytes** are likely to recognize the residual **malignant** cells after **surgical** removal of solid tumour, so these cells were adoptively transferred in conjunction with **surgery**. It has been observed in such experiments, the reappearance of tumour was **prevented** in 67% of mice and the survival of the hosts increased.
...MAJOR CONCEPTS: **Tumor** Biology

15/3,K,AB/15 (Item 4 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

10992816 BIOSIS NO.: 199799613961

Tumor-infiltration lymphocytes in combination with low-dose interleukin-2 in the treatment of 20 advanced cancers.

AUTHOR: Yao De-Mao Pan Cheng-En; Wang Yi-Li; et al

AUTHOR ADDRESS: First Hosp., Xi'an Med. Univ., Xi'an 710061**China

JOURNAL: Zhongguo Zhongliu Linchuang 24 (5):p339-342 1997

ISSN: 1000-8179

RECORD TYPE: Abstract

LANGUAGE: Chinese; Non-English

SUMMARY LANGUAGE: Chinese; English

ABSTRACT: Twenty cases of advanced cancers of stomach, liver, bladder were treated with **activated** auto-tumor-infiltrating **lymphocytes** (TIL) isolated from the patients themselves and supplemented by recombinant interleukin-2 (rIL-2). Cellular immune response was assayed before and after TIL infusion. The results revealed that cytotoxicity was much elevated (P lt 0.05). There was no significant change in cytotoxicity to histologically unrelated target cell lines (P gt 0.05). Serum IL-2 level was elevated markedly (12.3 U/ml to 19.8 U/ml, P lt 0.01). PHA skin test turned positive and the skin reaction lesion enlarged (PHA: 8, 6 mm to 13.5 mm, P lt 0.01). Eleven patients had transient chill and fever (T lt 38 degree C); and mild nausea and vomiting were seen in 6 of them during the TIL infusion. All these results indicate that TIL plus low-dose rIL-2 are able to improve cellular immunity in patients with advanced **cancer** without

side-effect. It may play an important role in **preventing** recurrence and metastasis.

1997

Tumor-infiltration lymphocytes in combination with low-dose interleukin-2 in the treatment of 20 advanced...

1997

ABSTRACT: Twenty cases of advanced cancers of stomach, liver, bladder were treated with **activated** auto-**tumor**-infiltrating **lymphocytes** (TIL) isolated from the patients themselves and supplemented by recombinant interleukin-2 (rIL-2). Cellular...

...plus low-dose rIL-2 are able to improve cellular immunity in patients with advanced **cancer** without side-effect. It may play an important role in **preventing** recurrence and metastasis.

MISCELLANEOUS TERMS: ...**BLADDER CANCER**; ...

...**CHEMOTHERAPY**; ...

...**LIVER CANCER**; ...

...**STOMACH CANCER**; ...

...**TUMOR-INFILTRATING LYMPHOCYTE THERAPY**

15/3,K,AB/16 (Item 5 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

10196955 BIOSIS NO.: 199698651873

Adoptive transfer of bryostatin-**activated tumor**-sensitized **lymphocytes** **prevents** or destroys **tumor** metastases without expansion in vitro.

AUTHOR: Fleming Martin D; Bear Harry D(a); Lipshy Kenneth; Kostuchenko Paul J; Portocarero Diana; McFadden Andrew W J; Barrett Sandra K

AUTHOR ADDRESS: (a)Div. Surgical Oncology, Box 980011, MCV Station, Medical College Virginia, Richmond, VA 23298**USA

JOURNAL: Journal of Immunotherapy with Emphasis on Tumor Immunology 18 (3):p147-155 1995

ISSN: 1067-5582

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Because the requirement for long-term cell culture can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor**-sensitized T cells activated briefly with bryostatin 1 and ionomycin (B/I) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas were harvested and treated for 18 h with B/I. These cells were then washed and transferred immediately to naive C57Bl/6 mice. In some experiments, these mice were irradiated (500 rads) before adoptive transfer and were given interleukin-2 (IL-2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated lymphocytes**. Recipient mice were challenged with sarcoma cells (4 times 10⁻⁵ i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10⁻⁶ B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous IL-2 or host irradiation. Using Thy-1

congenic donors, it was shown that B/I-activated T cells expanded in recipients when IL-2 was also given, and these cells were a prominent component (15% of total cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-"pulsed" cells with cyclophosphamide (CYP) and IL-2 to treat mice with established (3-day) metastases resulted in significant reduction in pulmonary nodules, with complete regression in many of the treated mice, which was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor**-sensitized, B/I-activated DLN cells confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor cells activated with B/I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

1995

Adoptive transfer of bryostatin-activated **tumor**-sensitized **lymphocytes** prevents or destroys **tumor** metastases without expansion in vitro.

1995

...ABSTRACT: can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor**-sensitized T cells activated briefly with bryostatin 1 and ionomycin (B/1) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas...

...2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated lymphocytes**. Recipient mice were challenged with sarcoma cells (4 times 10⁵ i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10⁶ B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous...

...cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-"pulsed" cells with cyclophosphamide (CYP) and IL-2 to treat...

...was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor**-sensitized, B/I-activated DLN cells confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor...

...I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

...MAJOR CONCEPTS: **Tumor** Biology

MISCELLANEOUS TERMS: ...POPLITEAL **TUMOR**-DRAINING LYMPH NODE...

...**TUMOR** IMMUNOLOGY

15/3,K,AB/17 (Item 6 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

08960750 BIOSIS NO.: 199396112251

A novel 80-kD cell surface structure identifies human circulating

lymphocytes with natural killer activity.
AUTHOR: Maiza Hassina; Leca Gerald; Mansur Indra-Gusti; Schiavon Valerie;
Boumsell Laurence; Bensussan Armand(a)
AUTHOR ADDRESS: (a)INSERM U93, Hospital Saint-Louis, 1 Ave. Claude
Vellefaux, 75475 Paris Cedex 10**France
JOURNAL: Journal of Experimental Medicine 178 (3):p1121-1126 1993
ISSN: 0022-1007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human lymphocytes with natural killer (NK) activity, including most **activated** gamma/delta+ T **lymphocytes**, recognize and lyse **tumor** target cells without requiring recognition of major histocompatibility complex antigen. However, unlike gamma/delta+ T lymphocytes, NK cells do not express CD3/T cell receptor (TCR) molecules, and the receptors involved in cell-mediated cytotoxicity are unknown. To further delineate circulating NK cells, we developed monoclonal antibodies (mAbs) against the human NK leukemia YT2C2. We report the isolation of a mAb termed BY55, recognizing at the cell surface a novel 80-kD protein with restricted expression. In addition to the immunizing cell line, this mAb binds to circulating NK cells, gamma/delta+ cells, and a minor subset of alpha/beta+ T lymphocytes. Expression of the BY55 mAb-reactive epitope/ molecule is regulated by activation, as short-term culture of peripheral blood lymphocytes (PBL) with phorbol ester induced its downmodulation. Furthermore, BY55 mAb reactivity was found neither with the NK nor with the TCR, alpha/beta+ and gamma/delta+ clones tested. Biochemical studies as well as phenotypic analysis revealed that this structure is different from all previously identified molecules on the lymphocyte cell surface. Interestingly, we found that BY55+ cells exert most NK activity obtained with fresh circulating lymphocytes. We report that within fresh E rosette-positive PBL only a subset of the CD16+, CD56+, and CD57+ cells coexpressed BY55 molecule, indicating that BY55 mAb defines a unique subset mediating NK activity of circulating PBL.

1993

1993

ABSTRACT: Human lymphocytes with natural killer (NK) activity, including most **activated** gamma/delta+ T **lymphocytes**, recognize and lyse **tumor** target cells without requiring recognition of major histocompatibility complex antigen. However, unlike gamma/delta+ T...
MISCELLANEOUS TERMS: ...**CHEMOTHERAPY** ASSOCIATED HEMATOPOIETIC
PROGENITOR CELL CYTOTOXICITY **PREVENTION** POTENTIAL

15/3,K,AB/18 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

09923640 Genuine Article#: 464YB Number of References: 89
Title: Hepatocellular **carcinoma**: an overview (ABSTRACT AVAILABLE)
Author(s): Anthony PP (REPRINT)
Corporate Source: Royal Devon & Exeter Hosp, Dept Histopathol, Exeter EX2
5AD/Devon/England/ (REPRINT); Royal Devon & Exeter Healthcare NHS
Trust, Dept Histopathol, Exeter/Devon/England/
Journal: HISTOPATHOLOGY, 2001, V39, N2 (AUG), P109-118
ISSN: 0309-0167 Publication date: 20010800
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE,
OXON, ENGLAND
Language: English Document Type: REVIEW
Abstract: Hepatocellular **carcinoma** remains widely prevalent in
tropical Africa and south-east Asia and is largely related to chronic

hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour incidence cannot be expected for decades to come yet, even in those countries in which the necessary resources exist, as millions of adults remain chronically infected. Meanwhile, the incidence is rising in Japan, Mediterranean countries of Europe, Middle East and North Africa and in the USA, largely due to chronic hepatitis C virus (HCV) infection introduced by the indiscriminate use of unscreened blood and blood products in the recent past. Much has been learned from molecular biological studies on hepatocarcinogenesis incriminating the HBX gene of HBV, the core protein of HCV and a unique guanine to thymine transversion at codon 249 has been observed in cases due to aflatoxin exposure. The subject of precancerous lesions, notably adenomatous/dysplastic nodules and large-cell/small-cell change continues to be a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases.

Title: Hepatocellular **carcinoma**: an overview
, 2001

Abstract: Hepatocellular **carcinoma** remains widely prevalent in tropical Africa and south-east Asia and is largely related to chronic hepatitis B virus (HBV) infection. Primary **prevention** by vaccination of infants at or near birth is effective but any reduction in tumour...

...a source of much debate and the distinction of nodular lesions in cirrhosis from early **carcinoma** remains uncertain. Spontaneous regression of hepatocellular **carcinoma** is rare but it is probably immunologically mediated and treatment by **activated T-lymphocytes** may reduce recurrence rates after **surgery**. The positive identification of hepatocellular **carcinoma** by a liver-specific antibody has greatly facilitated the diagnosis in difficult cases....

15/3,K,AB/19 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

09858633 Genuine Article#: 458MU Number of References: 45

Title: National Oncology Forum: Perspectives for the year 2000 (ABSTRACT AVAILABLE)

Author(s): DeVita VT (REPRINT) ; Bleickardt EW

Corporate Source: Yale Univ,Ctr Canc,470 Congress Ave,Suite 110-E/New Haven//CT/06519 (REPRINT); Yale Univ,Ctr Canc,New Haven//CT/06519; Yale Univ,Sch Med,New Haven//CT/06519

Journal: CANCER JOURNAL, 2001, V7, 1 (JUL-AUG), PS2-S13

ISSN: 1528-9117 Publication date: 20010700

Publisher: JONES AND BARTLETT PUBLISHERS, 40 TALL PONE DR, SUDBURY, MA 01776 USA

Language: English Document Type: ARTICLE

Abstract: Despite advances in treatment, long-term outcome of patients with diffuse large B cell lymphoma (DLBCL) is no better today than reported in 1975. A recent study applying DNA microarray technology revealed that patients whose **cancer** related to patterns of genes expressed in germinal center lymphocytes responded more favorably to **chemotherapy** than patients whose **cancer** related to patterns of genes expressed in **activated lymphocytes**. cDNA and oligonucleotide microarrays are described, and their applications in

cancer research are reviewed. In addition to DLBCL, microarray technology has been used to study several types of **cancer**. The applications of microarray technology are numerous and include profiling gene expression patterns in order to facilitate diagnosis and predict response to therapy; correlating patterns of gene expression with prognosis; and identifying genes and gene products that are associated with tumorigenic phenotype or with drug resistance, among other applications. Microarray technology has also been used in cell lines to correlate gene expression and **chemotherapy** response. Furthermore, microarray technology may provide a useful tool to examine the development of drug resistance in **cancer** and has recently been used to study changes in gene expression caused by activated c-Myc in primary human fibroblasts. Tissue microarrays are described. In addition to the amplification of limited tissue resources, tissue microarrays have the advantages of limiting the variability associated with tissue processing and limiting the necessary amount of reagent. Tissue microarrays have been used to determine the frequencies of amplification of 3 major breast **cancer** genes and identify overexpression of ERBB2 mRNA; assess and compare gene amplification in benign prostatic hyperplasia, primary prostate **carcinoma**, recurrent prostate tumors, and metastatic tumors; compare aggressiveness of prostate **carcinoma** in 2 patient populations; and study gene amplification across various **tumor** types. Furthermore, DNA microarray and tissue microarray techniques can be combined to provide convergent evidence of findings and to examine different aspects of gene expression. DNA array technology may also be used to identify critical molecular targets or to identify the critical rate-limiting step in a cascade of genes under the influence of a mutated gene. The historical progression of goals of the National **Cancer** Institute is reviewed, as well as the economic impact of reduction in **cancer**-associated mortality. Future efforts should continue the investment in basic research and more effectively integrate it with clinical trials and with approaches to **prevention** and treatment.

, 2001

- ...Abstract: then reported in 1975. A recent study applying DNA microarray technology revealed that patients whose **cancer** related to patterns of genes expressed in germinal center lymphocytes responded more favorably to **chemotherapy** than patients whose **cancer** related to patterns of genes expressed in **activated lymphocytes**. cDNA and oligonucleotide microarrays are described, and their applications in **cancer** research are reviewed. In addition to DLBCL, microarray technology has been used to study several types of **cancer**. The applications of microarray technology are numerous and include profiling gene expression patterns in order...
- ...applications. Microarray technology has also been used in cell lines to correlate gene expression and **chemotherapy** response. Furthermore, microarray technology may provide a useful tool to examine the development of drug resistance in **cancer** and has recently been used to study changes in gene expression caused by activated c...
- ...Tissue microarrays have been used to determine the frequencies of amplification of 3 major breast **cancer** genes and identify overexpression of ERBB2 mRNA; assess and compare gene amplification in benign prostatic hyperplasia, primary prostate **carcinoma**, recurrent prostate tumors, and metastatic tumors; compare aggressiveness of prostate **carcinoma** in 2 patient populations; and study gene amplification across various **tumor** types. Furthermore, DNA microarray and tissue microarray techniques can be combined to provide convergent evidence...
- ...under the influence of a mutated gene. The historical progression of

goals of the National Cancer Institute is reviewed, as well as the economic impact of reduction in cancer-associated mortality. Future efforts should continue the investment in basic research and more effectively integrate it with clinical trials and with approaches to **prevention** and treatment.

...Identifiers--DIFFERENTIALLY EXPRESSED GENES; OLIGONUCLEOTIDE ARRAYS; TISSUE MICROARRAYS; PROSTATE-CANCER; MOLECULAR CLASSIFICATION; COMPLEMENTARY-DNA; CDNA MICROARRAYS; CELL-CYCLE; **TUMOR**; REVEALS

15/3,K,AB/20 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

07876118 Genuine Article#: 219PJ Number of References: 77
Title: Bcl-2-mediated drug resistance: Inhibition of apoptosis by blocking nuclear factor of **activated T lymphocytes** (NFAT)-induced Fas ligand transcription (ABSTRACT AVAILABLE)
Author(s): Srivastava RK (REPRINT) ; Sasaki CY; Hardwick JM; Longo DL
Corporate Source: NIA,IMMUNOL LAB, NIH, 5600 NATHAN SHOCK DR, BOX 9/BALTIMORE//MD/21224 (REPRINT); JOHNS HOPKINS UNIV,SCH PUBL HLTH, DEPT MOL BIOL & IMMUNOL/BALTIMORE//MD/21205
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, 1999, V190, N2 (JUL 19), P 253-265
ISSN: 0022-1007 Publication date: 19990719
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021

Language: English Document Type: ARTICLE

Abstract: Bcl-2 inhibits apoptosis induced by a variety of stimuli, including **chemotherapy** drugs and glucocorticoids. It is generally accepted that Bcl-2 exerts its antiapoptotic effects mainly by dimerizing with proapoptotic members of the Bcl-2 family such as Bar and Bad. However, the mechanism of the antiapoptotic effects is unclear. Paclitaxel and other drugs that disturb microtubule dynamics kill cells in a Fas/Fas ligand (FasL)-dependent manner; antibody to FasL inhibits paclitaxel-induced apoptosis. We have found that Bcl-2 overexpression leads to the **prevention of chemotherapy** (paclitaxel)-induced expression of Fas and blocks paclitaxel-induced apoptosis. The mechanism of this effect is that Bcl-2 **prevents** the nuclear translocation of NFAT (nuclear factor of **activated T lymphocytes**, a transcription factor **activated** by microtubule damage) by binding and sequestering calcineurin, a calcium-dependent phosphatase that must dephosphorylate NFAT to move to the nucleus. Without NFAT nuclear translocation, the Fas gene is not transcribed. Thus, it appears that paclitaxel and other drugs that disturb microtubule function kill cells at least in part through the induction of FasL. Furthermore, Bcl-2 antagonizes drug-induced apoptosis by inhibiting calcineurin activation, blocking NFAT nuclear translocation, and **preventing** Fas expression. The effects of Bcl-2 can be overcome, at least partially, through phosphorylation of Bcl-2. Phosphorylated Bcl-2 cannot bind calcineurin, and NFAT activation, Fas expression, and apoptosis can occur after Bcl-2 phosphorylation.

Title: Bcl-2-mediated drug resistance: Inhibition of apoptosis by blocking nuclear factor of **activated T lymphocytes** (NFAT)-induced Fas ligand transcription
, 1999

Abstract: Bcl-2 inhibits apoptosis induced by a variety of stimuli, including **chemotherapy** drugs and glucocorticoids. It is generally accepted that Bcl-2 exerts its antiapoptotic effects mainly...

...FasL inhibits paclitaxel-induced apoptosis. We have found that Bcl-2 overexpression leads to the **prevention of chemotherapy**

(paclitaxel)-induced expression of Fas and blocks paclitaxel-induced apoptosis. The mechanism of this effect is that Bcl-2 **prevents** the nuclear translocation of NFAT (nuclear factor of **activated T lymphocytes**, a transcription factor **activated** by microtubule damage) by binding and sequestering calcineurin, a calcium-dependent phosphatase that must dephosphorylate...

...Bcl-2 antagonizes drug-induced apoptosis by inhibiting calcineurin activation, blocking NFAT nuclear translocation, and **preventing** Fas expression. The effects of Bcl-2 can be overcome, at least partially, through phosphorylation...

...Identifiers--CD95 APO-1/FAS SYSTEM; INDUCED CELL-DEATH; CYCLOSPORINE-A; **CANCER-CELLS**; NF-AT; MEDIATED TRANSCRIPTION; BCL2 PHOSPHORYLATION; ENDOTHELIAL-CELLS; DEFICIENT MICE; IMMUNE EVASION

15/3,K,AB/21 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

07822724 Genuine Article#: 212BL Number of References: 47
Title: Fas-FasL-mediated CD4+T-cell apoptosis following stem cell transplantation (ABSTRACT AVAILABLE)
Author(s): Singh RK; Varney ML; Buyukberber S; Ino K; Ageitos AG; Reed E; Tarantolo S; Talmadge JE (REPRINT)
Corporate Source: UNIV NEBRASKA,MED CTR, DEPT PATHOL & MICROBIOL, 985660 NEBRASKA MED CTR/OMAHA//NE/68198 (REPRINT); UNIV NEBRASKA,MED CTR, DEPT PATHOL & MICROBIOL/OMAHA//NE/68198; UNIV NEBRASKA,MED CTR, DEPT INTERNAL MED ONCOL HEMATOL/OMAHA//NE/68198
Journal: CANCER RESEARCH, 1999, V59, N13 (JUL 1), P3107-3111
ISSN: 0008-5472 Publication date: 19990701
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202
Language: English Document Type: ARTICLE

Abstract: We report the preferential expression of Fas; on CD4(+) T cells and Fas Ligand (FasL) on monocytes and their potential role in the selective loss of CD4(+) T cells in breast **cancer** patients underlying high-dose **chemotherapy**, and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4(+) T cells (28-51%) is observed during the first 100 days after PSCT concomitant with a significant increase in monocyte frequency and FasL expression (11.6-23%) on monocytes. The preferential expression of Fas on CD4(+) T cells (73-92%) in the peripheral blood (PB) of these patients is associated with a significantly higher frequency of CD4(+) T-cell apoptosis compared with CD8(+) T cells (28-47%) and CD4(+) T cells (46 +/- 5.7%) in normal PB. These data suggest that 'primed' Fas(+) CD4(+) **lymphocytes** interact with **activated** monocytes that express Fas, resulting in apoptosis, leading to deletion of CD4(+) T cells, an inversion in the CD4:CD8 T-cell ratio, and immune dysfunction. The **prevention** of CD4(+) T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem cell products, blockade of Fas-FasL interactions, or cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

, 1999

...Abstract: monocytes and their potential role in the selective loss of CD4(+) T cells in breast **cancer** patients underlying high-dose **chemotherapy**, and peripheral blood stem cell transplantation (PSCT). A high frequency of apoptotic CD4(+) T cells...

...T cells (46 +/- 5.7%) in normal PB. These data suggest that 'primed' Fas(+) CD4(+) **lymphocytes** interact with **activated** monocytes that express Fas, resulting in apoptosis, leading to deletion of CD4(+) T cells, an inversion in the CD4:CD8 T-cell ratio, and immune

dysfunction. The **prevention** of CD4(+) T-cell apoptosis and improved immune reconstitution by the manipulation of PB stem...

...cytokine support after transplantation may be important adjuvant immunotherapeutic strategies in patients undergoing high-dose **chemotherapy** and PSCT.

15/3,K,AB/22 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

06015228 Genuine Article#: XP442 Number of References: 25
Title: Homing of polyclonally activated syngeneic T cells at tumour site and their efficacy in post operative immunotherapy of **malignancy** in mouse (ABSTRACT AVAILABLE)
Author(s): Chakravarty AK (REPRINT) ; Jha S
Corporate Source: N BENGAL UNIV,CTR LIFE SCI, IMMUNOL & CELL BIOL LAB/DARJEELING 734430//INDIA/ (REPRINT)
Journal: CURRENT SCIENCE, 1997, V73, N2 (JUL 25), P201-203
ISSN: 0011-3891 Publication date: 19970725
Publisher: CURRENT SCIENCE ASSN, C V RAMAN AVENUE, PO BOX 8005, BANGALORE 560 080, INDIA
Language: English Document Type: ARTICLE
Abstract: H-3-Thymidine labelled and polyclonally **activated** syngeneic **lymphocytes** injected intravenously have been found to home preferentially at the fibrosarcoma site in mice from 12 h after adoptive transfer. The highest counts from infiltrating radiolabelled cells were obtained at 24 h at the centre of the tumour. Considering this value as maximum, all other values are expressed relative to this number. At 12 h lymphocyte infiltration at the periphery of the tumour mass was about 75%, followed by about 40% infiltration in the liver. After 24 h the central region of tumour mass showed the highest infiltration of radioactively labelled lymphocytes, whereas in liver it remained 50%. There was decline in homing of the **activated lymphocytes** after 48 h of adoptive transfer.

These tumour site seeking **activated lymphocytes** are likely to recognize the residual **malignant** cells after **surgical** removal of solid tumour, so these cells were adoptively transferred in conjunction with **surgery**. It has been observed in such experiments, the reappearance of tumour was **prevented** in 67% of mice and the survival of the hosts increased.

...Title: activated syngeneic T cells at tumour site and their efficacy in post operative immunotherapy of **malignancy** in mouse
, 1997

Abstract: H-3-Thymidine labelled and polyclonally **activated** syngeneic **lymphocytes** injected intravenously have been found to home preferentially at the fibrosarcoma site in mice from...

...labelled lymphocytes, whereas in liver it remained 50%. There was decline in homing of the **activated lymphocytes** after 48 h of adoptive transfer.

These tumour site seeking **activated lymphocytes** are likely to recognize the residual **malignant** cells after **surgical** removal of solid tumour, so these cells were adoptively transferred in conjunction with **surgery**. It has been observed in such experiments, the reappearance of tumour was **prevented** in 67% of mice and the survival of the hosts increased.

15/3,K,AB/23 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

05068280 Genuine Article#: TN419 Number of References: 27

Title: ADOPTIVE TRANSFER OF BRYOSTATIN-**ACTIVATED TUMOR**

-SENSITIZED **LYMPHOCYTES PREVENTS OR DESTROYS TUMOR**

-METASTASES WITHOUT EXPANSION IN-VITRO (Abstract Available)

Author(s): FLEMING MD; BEAR HD; LIPSHY K; KOSTUCHENKO PJ; PORTOCARERO D;
MCFADDEN AWJ; BARRETT SK

Corporate Source: VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DIV SURG
ONCOL, DEPT SURG, BOX 980011, MCV STN/RICHMOND//VA/23298; VIRGINIA
COMMONWEALTH UNIV, MED COLL VIRGINIA, DIV SURG ONCOL, DEPT
SURG/RICHMOND//VA/23298; VIRGINIA COMMONWEALTH UNIV, MED COLL
VIRGINIA, MASSEY CANC CTR/RICHMOND//VA/23298; SE ONCOL
GRP/MEMPHIS//TN/00000; UNIV SASKATCHEWAN/SASKATOON/SK/CANADA/

Journal: JOURNAL OF IMMUNOTHERAPY, 1995, V18, N3 (OCT), P147-155

ISSN: 1053-8550

Language: ENGLISH Document Type: ARTICLE

Abstract: Because the requirement for long-term cell culture can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor-sensitized T cells** activated briefly with bryostatin 1 and ionomycin (B/T) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas were harvested and treated for 18 h with B/I. These cells were then washed and transferred immediately to naive C57BI/6 mice. In some experiments, these mice were irradiated (500 rads) before adoptive transfer and were given interleukin-2 (IL-2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated lymphocytes**. Recipient mice were challenged with sarcoma cells (4 x 10⁵ i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10⁶ B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous IL-2 or host irradiation. Using Thy-1 congenic donors, it was shown that B/I-activated T cells expanded in recipients when IL-2 was also given, and these cells were a prominent component (15% of total cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-'pulsed' cells with cyclophosphamide (CYP) and IL-2 to treat mice with established (3-day) metastases resulted in significant reduction in pulmonary nodules, with complete regression in many of the treated mice, which was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor-sensitized, B/I-activated DLN cells** confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor cells activated with B/I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

Title: ADOPTIVE TRANSFER OF BRYOSTATIN-**ACTIVATED TUMOR**

-SENSITIZED **LYMPHOCYTES PREVENTS OR DESTROYS TUMOR**

-METASTASES WITHOUT EXPANSION IN-VITRO

, 1995

...Abstract: can make adoptive cellular immunotherapy cumbersome, experiments were designed to determine whether smaller numbers of **tumor-sensitized T cells** activated briefly with bryostatin 1 and ionomycin (B/T) could be returned immediately to recipient mice without in vitro expansion and still have an anti-**tumor** effect in vivo. Popliteal **tumor**-draining lymph nodes (DLNs) from mice bearing progressive MCA-105 and MCA-203 footpad sarcomas...

...2, 7,500 IU i.p., b.i.d. for 3 days) after receiving the **activated**

lymphocytes. Recipient mice were challenged with sarcoma cells (4 x 10⁵) i.v.) 6 to 32 days after receiving the **activated lymphocytes**. Mice receiving 10⁶) B/I-**activated lymphocytes** before **tumor** challenge had significantly fewer metastases than did controls. This protective effect did not require exogenous...

...cells) in the infiltrates found in the lungs of mice 7 days after i.v. **tumor** challenge. Combining these B/I-'pulsed' cells with cyclophosphamide (CYP) and IL-2 to treat...

...was rarely seen with CYP alone or with CYP + IL-2. Thus, adoptive transfer of **tumor**-sensitized, B/I-activated DLN cells confers protection against i.v. **tumor** challenge, without prior in vitro expansion of the effector cells. Phenotyping studies demonstrate that donor...

...I do expand in recipient mice after adoptive transfer and can move to sites of **tumor**. Moreover, these cells can mediate a therapeutic effect on established **tumor** metastases, when combined with **chemotherapy**.

...Identifiers--DRAINING LYMPH-NODES; T-CELLS; INFILTRATING LYMPHOCYTES; ESTABLISHED TUMORS; MURINE **TUMOR**; IMMUNOTHERAPY; INVITRO; INTERLEUKIN-2; REGRESSION; MELANOMA

Research Fronts: 94-1902 002 (**TUMOR**-INFILTRATING LYMPHOCYTES; T-CELL RECEPTOR; METASTATIC MELANOMA)

15/3,K,AB/24 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

04991520 Genuine Article#: UX719 Number of References: 226
Title: RECENT ADVANCES IN THE TREATMENT OF NONSMALL CELL LUNG-**CANCER**
(Abstract Available)
Author(s): GOSS GD; DAHROUGE S; LOCHRIN CA
Corporate Source: UNIV OTTAWA, FAC MED, OTTAWA REG CANC CTR, ONTARIO CANC
TREATMENT & RES FDN, 501 SMYTH RD/OTTAWA/ONK1H 8L6/CANADA/
Journal: ANTI-CANCER DRUGS, 1996, V7, N4 (JUN), P363-385
ISSN: 0959-4973

15/3,K,AB/24 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

04991520 Genuine Article#: UX719 Number of References: 226
Title: RECENT ADVANCES IN THE TREATMENT OF NONSMALL CELL LUNG-CANCER
(Abstract Available)
Author(s): GOSS GD; DAHROUGE S; LOCHRIN CA
Corporate Source: UNIV OTTAWA, FAC MED, OTTAWA REG CANC CTR, ONTARIOCANC
TREATMENT & RES FDN, 501 SMYTH RD/OTTAWA/ONK1H 8L6/CANADA/
Journal: ANTI-CANCER DRUGS, 1996, V7, N4 (JUN), P363-385
ISSN: 0959-4973
Language: ENGLISH Document Type: REVIEW

Abstract: Non-small cell lung **cancer** (NSCLC), which represents the bulk of primary carcinomas of the lung, is an aggressive **malignancy**. The majority of patients with NSCLC present with advanced disease, not curable by **surgery**, at the time of diagnosis. Recent randomized trials have shown an improvement in survival for patients with loco-regional disease treated with combination, platinum-based, **chemotherapy** and curative irradiation. Similarly, randomized studies of good performance status patients with metastatic disease have documented a survival advantage, albeit a modest advantage, for those receiving **chemotherapy**. New **chemotherapy** agents with activity in NSCLC have been studied in phase II trials. These agents need to be evaluated, in loco-regional and metastatic disease, in large randomized phase III trials before conclusions can be drawn about their role in treatment. Novel treatments which among others include gene therapy, anti-angiogenic and anti-metastatic agents are currently being assessed in early phase I and II studies. Gene therapy will likely be combined with standard **chemotherapy** and radiation in the treatment of NSCLC, whereas anti-angiogenic and anti-metastatic agents may play a role in **prevention** and maintenance therapy. Finally, regardless of the approach or modality, new interventions will need to be assessed for their impact on overall survival and the quality of life of patients with NSCLC.

Title: RECENT ADVANCES IN THE TREATMENT OF NONSMALL CELL LUNG-CANCER
, 1996

Abstract: Non-small cell lung **cancer** (NSCLC), which represents the bulk of primary carcinomas of the lung, is an aggressive **malignancy**. The majority of patients with NSCLC present with advanced disease, not curable by **surgery**, at the time of diagnosis. Recent randomized trials have shown an improvement in survival for patients with loco-regional disease treated with combination, platinum-based, **chemotherapy** and curative irradiation. Similarly, randomized studies of good performance status patients with metastatic disease have documented a survival advantage, albeit a modest advantage, for those receiving **chemotherapy**. New **chemotherapy** agents with activity in NSCLC have been studied in phase II trials. These agents need...

...in early phase I and II studies. Gene therapy will likely be combined with standard **chemotherapy** and radiation in the treatment of NSCLC, whereas anti-angiogenic and anti-metastatic agents may play a role in **prevention** and maintenance therapy. Finally, regardless of the approach or modality, new interventions will need to...

...Identifiers--TYPE P53; MULTICENTER RANDOMIZED TRIAL;
THERAPY-ONCOLOGY-GROUP; DIRECT GENE-TRANSFER; PHASE-II TRIAL;
COMBINATION **CHEMOTHERAPY**; VINORELBINE NAVELBINE;
RADIATION-THERAPY; SUPPORTIVE CARE; IV COLLAGENASE
Research Fronts: 94-0176 010 (NONSMALL CELL LUNG-CANCER;
CHEMOTHERAPY PLUS RADICAL RADIOTHERAPY; SEQUENCE SPECIFICITY OF

DRUG-STIMULATED TOPOISOMERASE-II DNA CLEAVAGE)
94-0971 006...

...CADHERIN EXPRESSION; EXTRACELLULAR DOMAIN OF PEMPHIGUS-VULGARIS ANTIGEN
(DESMOGLEIN-3) MEDIATES WEAK HEMOPHILIC ADHESION; TONGUE
CARCINOMA CELL-LINES)
94-1311 001 (T-CELL COSTIMULATORY MOLECULE; **ACTIVATED** MURINE B-
LYMPHOCYTES; FUNCTIONAL EXPRESSION; TRANSGENIC MICE; CD28
CO-STIMULATION; SOLUBLE CTLA-4)
94-1630 001 (P53 **TUMOR**-SUPPRESSOR GENE; RETINOBLASTOMA PROTEIN;
CELL-CYCLE PROGRESSION)
94-1777 001 (NECK TUMORS; RADIOTHERAPY TREATMENT TIME; LOCAL-CONTROL
RATES FOR EARLY GLOTTIC **CARCINOMA**; ACCELERATED RADIATION-THERAPY;
THYMIDINE REPLACEMENT)
94-8400 001 (DIRECT DNA INJECTION; VACCINE DELIVERY; IN-VIVO...

15/3,K,AB/25 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

04834203 Genuine Article#: UL209 Number of References: 38
Title: INFLAMMATORY CELLS INFILTRATING HUMAN COLORECTAL CARCINOMAS EXPRESS
HLA CLASS-II BUT NOT B7-1 AND B7-2 COSTIMULATORY MOLECULES OF THE
T-CELL ACTIVATION (Abstract Available)
Author(s): CHAUX P; MOUTET M; FAIVRE J; MARTIN F; MARTIN M
Corporate Source: FAC MED,DEPT BIOL & THERAPY CANC,7 BD JEANNE DARC/F-21033
DIJON//FRANCE/; FAC MED,DEPT BIOL & THERAPY CANC/F-21033 DIJON//FRANCE/
; FAC MED,DIGEST CANC REGISTRY BURGUNDY/F-21033 DIJON//FRANCE/
Journal: LABORATORY INVESTIGATION, 1996, V74, N5 (MAY), P975-983
ISSN: 0023-6837

Language: ENGLISH Document Type: ARTICLE

Abstract: Colon **cancer** cells express potentially immunogenic proteins
but are not rejected by the immune system. To induce an effective
immune response, antigenic peptides have to be presented to T
lymphocytes by professional antigen-presenting cells in association
with HLA class II molecules. Antigen-presenting cells also have to
express B7 family molecules, B7-1 and B7-2, which deliver the
costimulatory signals that are required to **prevent** T cell anergy.
We studied B7-1 and B7-2 expression by the antigen-presenting cells
that infiltrate colorectal **cancer** stroma. In 25 samples of
colorectal carcinomas, a panel of monoclonal antibodies was used to
label macrophages, dendritic cells, and T lymphocytes that infiltrate
the **tumor** stroma and the morphologically normal distant mucosa.
The expression of HLA class II and B7 molecules involved in T-cell
activation was studied using specific monoclonal antibodies. Biopsy
pieces from two patients with active Crohn's disease were used as
controls. All of the samples were heavily infiltrated by macrophages
and/or dendritic cells that strongly expressed HLA class II molecules.
In contrast, antibodies to B7-1 and/or B7-2 stained no cells in 16 of
the 25 samples of colorectal tumors and less than 1% of the
inflammatory cells that infiltrated **tumor** stroma of the other
nine **tumor** samples. B7 molecules were also poorly expressed by
rare cells in the lamina propria of the morphologically normal
colorectal mucosa. In contrast, many inflammatory cells that
infiltrated the two Crohn's disease samples strongly expressed B7-1 and
B7-2, especially in the granulomas. We conclude that most HLA class II+
inflammatory cells that infiltrate colorectal cancers do not express
the B7-1 and B7-2 costimulatory molecules. This defect may contribute
to the failure of the immune system to recognize **tumor** cells as
antigenic.

, 1996

Abstract: Colon **cancer** cells express potentially immunogenic proteins

but are not rejected by the immune system. To induce...

...molecules, B7-1 and B7-2, which deliver the costimulatory signals that are required to **prevent** T cell anergy. We studied B7-1 and B7-2 expression by the antigen-presenting cells that infiltrate colorectal **cancer** stroma. In 25 samples of colorectal carcinomas, a panel of monoclonal antibodies was used to label macrophages, dendritic cells, and T lymphocytes that infiltrate the **tumor** stroma and the morphologically normal distant mucosa. The expression of HLA class II and B7...

...25 samples of colorectal tumors and less than 1% of the inflammatory cells that infiltrated **tumor** stroma of the other nine **tumor** samples. B7 molecules were also poorly expressed by rare cells in the lamina propria of...

...costimulatory molecules. This defect may contribute to the failure of the immune system to recognize **tumor** cells as antigenic.

Research Fronts: 94-1311 003 (T-CELL COSTIMULATORY MOLECULE;

ACTIVATED MURINE B-LYMPHOCYTES; FUNCTIONAL EXPRESSION;

TRANSGENIC MICE; CD28 CO-STIMULATION; SOLUBLE CTLA-4)

94-1351 001 (LOCAL RECURRENCE OF COLORECTAL-CANCER; LONG-TERM

SURVIVAL; CURATIVE **SURGERY**; LOW ANTERIOR RESECTION; STAGING

RECTAL-CARCINOMA)

15/3,K,AB/26 (Item 9 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

04714763 Genuine Article#: UC525 Number of References: 21

Title: VACCINATION OF **TUMOR**-CELLS TRANSFECTED WITH THE B7-1 (CD80)

GENE INDUCES THE ANTIMETASTATIC EFFECT AND **TUMOR**-IMMUNITY IN MICE

(Abstract Available)

Author(s): FUJII H; INOBE M; KIMURA F; MURATA J; MURAKAMI M; ONISHI Y;

AZUMA I; UEDE T; SAIKI I

Corporate Source: TOYAMA MED & PHARMACEUT UNIV, RES INST WAKAN YAKU TRADIT

SINO JAPANESE MED, 2630 SUGITANI/TOYAMA 93001//JAPAN/; TOYAMA MED &

PHARMACEUT UNIV, RES INST WAKAN YAKU TRADIT SINO JAPANESE MED/TOYAMA

93001//JAPAN/; HOKKAIDO UNIV, SECT IMMUNOPATHGENESIS/SAPPORO/HOKKAIDO

060/JAPAN/; HOKKAIDO UNIV, SECT CHEM, INST IMMUNOL SCI/SAPPORO/HOKKAIDO

060/JAPAN/

Journal: INTERNATIONAL JOURNAL OF CANCER, 1996, V66, N2 (APR 10), P

219-224

ISSN: 0020-7136

Language: ENGLISH Document Type: ARTICLE

Abstract: The present study demonstrates that the transfection of B7-1 or its variant MB7-2 genes into MHC class 1(+) **tumor** cells (B16-BL6 or K1735-M2 melanoma) resulted in the remarkable reduction of lung metastasis caused by i.v. injection into immunocompetent syngeneic mice. However, i.v. injection of the transfectants into T cell-deficient nude mice did not affect reduction of lung **tumor** colonies as compared with parental wild-type tumors, suggesting that such an inhibitory effect was closely associated with T cell-mediated responses. The reduced metastasis of B7(+) **tumor** cells consequently led to the significant prolongation of survival. Expression of B7 on **tumor** cells did not influence the tumorigenicity in vivo and **tumor** cell invasion into basement membrane Matrigel in vitro. We also found that immunization of X-irradiated by transfectants was effective as a **tumor** vaccine for **preventing** lung metastasis caused by i.v. injection of B7(-) parental B16-BL6 cells but not against other syngeneic 3LL tumors. Thus, the by-mediated anti-metastatic effect was **tumor**-specific. Vaccinations of irradiated B7(+) **tumor** cells before and after

surgical excision of the s.c. inoculated primary B7(-) tumors on day 21 achieved effectively the **prevention** of spontaneous lung metastasis. Our report that vaccination of irradiated B7(+) **tumor** cells led to a therapeutic effect in an established **tumor** metastasis model clearly expands and confirms previous related observations. (C) 1996 Wiley-Liss, Inc.

Title: VACCINATION OF **TUMOR**-CELLS TRANSFECTED WITH THE B7-1 (CD80) GENE INDUCES THE ANTIMETASTATIC EFFECT AND **TUMOR**-IMMUNITY IN MICE , 1996

...Abstract: the transfection of B7-1 or its variant MB7-2 genes into MHC class 1(+) **tumor** cells (B16-BL6 or K1735-M2 melanoma) resulted in the remarkable reduction of lung metastasis...

...of the transfectants into T cell-deficient nude mice did not affect reduction of lung **tumor** colonies as compared with parental wild-type tumors, suggesting that such an inhibitory effect was closely associated with T cell-mediated responses. The reduced metastasis of B7(+) **tumor** cells consequently led to the significant prolongation of survival. Expression of B7 on **tumor** cells did not influence the tumorigenicity in vivo and **tumor** cell invasion into basement membrane Matrigel in vitro. We also found that immunization of X-irradiated by transfectants was effective as a **tumor** vaccine for **preventing** lung metastasis caused by i.v. injection of B7(-) parental B16-BL6 cells but not against other syngeneic 3LL tumors. Thus, the by-mediated anti-metastatic effect was **tumor**-specific. Vaccinations of irradiated B7(+) **tumor** cells before and after **surgical** excision of the s.c. inoculated primary B7(-) tumors on day 21 achieved effectively the **prevention** of spontaneous lung metastasis. Our report that vaccination of irradiated B7(+) **tumor** cells led to a therapeutic effect in an established **tumor** metastasis model clearly expands and confirms previous related observations. (C) 1996 Wiley-Liss, Inc.

Research Fronts: 94-1311 005 (T-CELL COSTIMULATORY MOLECULE; **ACTIVATED** MURINE B-LYMPHOCYTES; FUNCTIONAL EXPRESSION; TRANSGENIC MICE; CD28 CO-STIMULATION; SOLUBLE CTLA-4)
94-0462 001 (INTEGRIN EXPRESSION...

15/3,K,AB/27 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

04630279 Genuine Article#: TX912 Number of References: 254
Title: THE FAILURE OF CURRENT IMMUNOTHERAPY FOR **MALIGNANT** GLIOMA - **TUMOR**-DERIVED TGF-BETA, T-CELL APOPTOSIS, AND THE IMMUNE PRIVILEGE OF THE BRAIN (Abstract Available)
Author(s): WELLER M; FONTANA A
Corporate Source: UNIV TUBINGEN,NEUROL KLIN,HOPPE SEYLER STR 3/D-72076 TUBINGEN//GERMANY/; UNIV SPITAL ZURICH,DEPT INNERE MED,ABT KLIN IMMUNOL/CH-8044 ZURICH//SWITZERLAND/
Journal: BRAIN RESEARCH REVIEWS, 1995, V21, N2 (SEP), P128-151
ISSN: 0165-0173
Language: ENGLISH Document Type: REVIEW

Abstract: Human **malignant** gliomas are rather resistant to all current therapeutic approaches including **surgery**, radiotherapy and **chemotherapy** as well as antibody-guided or cellular immunotherapy. The immunotherapy of **malignant** glioma has attracted interest because of the immunosuppressed state of **malignant** glioma patients which resides mainly in the T-cell compartment. This T-cell suppression has been attributed to the release by the glioma cells of immunosuppressive factors like transforming growth factor-beta (TGF-beta) and prostaglandins. TGF-beta has multiple effects in the immune system, most of which are inhibitory. TGF-beta

appears to control downstream elements of various cellular activation cascades and regulates the expression of genes that are essential for cell cycle progression and mitosis. Since TGF-beta-mediated growth arrest of T-cell lines results in their apoptosis in vitro, glioma-derived TGF-beta may **prevent** immune-mediated glioma cell elimination by inducing apoptosis of **tumor**-infiltrating lymphocytes in vivo. T-cell apoptosis in the brain may be augmented by the absence of professional antigen-presenting cells and of appropriate costimulating signals. Numerous in vitro studies predict that **tumor**-derived TGF-beta will incapacitate in vitro-expanded and locally administered lymphokine-activated killer cells (LAK-cells) or **tumor**-infiltrating lymphocytes. Thus, TGF-beta may be partly responsible for the failure of current adoptive cellular immunotherapy of **malignant** glioma. Recent experimental in vivo studies on non-glial tumors have corroborated that neutralization of **tumor**-derived TGF-beta activity may facilitate immune-mediated **tumor** rejection. Current efforts to improve the efficacy of immunotherapy for **malignant** glioma include various strategies to enhance the immunogenicity of glioma cells and the cytotoxic activity of immune effector cells, e.g., by cytokine gene transfer. Future strategies of cellular immunotherapy for **malignant** glioma will have to focus on rendering glioma cell-targeting immune cells resistant to local inactivation and apoptosis which may be induced by TGF-beta and other immunosuppressive molecules at the site of neoplastic growth. Cytotoxic effectors targeting Fas/APO-1, the receptor protein for perforin-independent cytotoxic T-cell killing, might be promising, since Fas/APO-1 is expressed by glioma cells but not by untransformed brain cells, and since Fas/APO-1-mediated killing in vitro is not inhibited by TGF-beta.

Title: THE FAILURE OF CURRENT IMMUNOTHERAPY FOR **MALIGNANT** GLIOMA -
TUMOR-DERIVED TGF-BETA, T-CELL APOPTOSIS, AND THE IMMUNE
 PRIVILEGE OF THE BRAIN
 , 1995

Abstract: Human **malignant** gliomas are rather resistant to all current therapeutic approaches including **surgery**, radiotherapy and **chemotherapy** as well as antibody-guided or cellular immunotherapy. The immunotherapy of **malignant** glioma has attracted interest because of the immunosuppressed state of **malignant** glioma patients which resides mainly in the T-cell compartment. This T-cell suppression has...

...of T-cell lines results in their apoptosis in vitro, glioma-derived TGF-beta may **prevent** immune-mediated glioma cell elimination by inducing apoptosis of **tumor**-infiltrating lymphocytes in vivo. T-cell apoptosis in the brain may be augmented by the...

...professional antigen-presenting cells and of appropriate costimulating signals. Numerous in vitro studies predict that **tumor**-derived TGF-beta will incapacitate in vitro-expanded and locally administered lymphokine-activated killer cells (LAK-cells) or **tumor**-infiltrating lymphocytes. Thus, TGF-beta may be partly responsible for the failure of current adoptive cellular immunotherapy of **malignant** glioma. Recent experimental in vivo studies on non-glial tumors have corroborated that neutralization of **tumor**-derived TGF-beta activity may facilitate immune-mediated **tumor** rejection. Current efforts to improve the efficacy of immunotherapy for **malignant** glioma include various strategies to enhance the immunogenicity of glioma cells and the cytotoxic activity...

...immune effector cells, e.g., by cytokine gene transfer. Future strategies of cellular immunotherapy for **malignant** glioma will have to focus on rendering glioma cell-targeting immune cells resistant to local...

Research Fronts: 94-1311 002 (T-CELL COSTIMULATORY MOLECULE;
ACTIVATED MURINE B-LYMPHOCYTES; FUNCTIONAL EXPRESSION;
TRANSGENIC MICE; CD28 CO-STIMULATION; SOLUBLE CTLA-4)
94-1346 002 (TRANSFORMING GROWTH...

...EXPRESSION IN MOUSE DENDRITIC CELL CLONES; NONSPECIFIC REGULATORY
MECHANISM OF CONTACT SENSITIVITY)

94-1902 002 (**TUMOR**-INFILTRATING LYMPHOCYTES; T-CELL RECEPTOR;
METASTATIC MELANOMA)

94-4226 002 (FAS ANTIGEN; REGULATION OF APOPTOSIS...

...EXPRESSION; ANDROGEN REGULATION)

94-4487 001 (HERPES-SIMPLEX THYMIDINE KINASE GENE GANCICLOVIR SYSTEM;
IN-VIVO **TUMOR** TRANSDUCTION; RAT GLIOMA-CELLS; RECOMBINANT
ADENOVIRUS; RETROVIRAL VECTORS)

94-5532 001 (CYTOKINE RECEPTOR MESSENGER-RNA...

15/3,K,AB/28 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

03926965 Genuine Article#: QT145 Number of References: 88
Title: ANTIMETASTATIC EFFECTS OF PSK (KRESTIN), A PROTEIN-BOUND
POLYSACCHARIDE OBTAINED FROM BASIDIOMYCETES - AN OVERVIEW (Abstract
Available)

Author(s): KOBAYASHI H; MATSUNAGA K; OGUCHI Y

Corporate Source: KUREHA CHEM IND CO LTD,BIOMED RES LAB,SHINJUKU KU,3-26-2
HYAKUNIN CHO/TOKYO 169//JAPAN/; KUREHA CHEM IND CO LTD,BIOMED RES
LAB,SHINJUKU KU/TOKYO 169//JAPAN/; HLTH SCI UNIV
HOKKAIDO/TOUBETU/HOKKAIDO 06102/JAPAN/

Journal: CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION, 1995, V4, N3 (
APR-MAY), P275-281

ISSN: 1055-9965

Language: ENGLISH Document Type: REVIEW

Abstract: PSK, a protein-bound polysaccharide obtained from cultured
mycelia of *Coriolus versicolor* in basidiomycetes, is a biological
response modifier, diverse operations of which include an antitumor
action. We have previously reviewed recent research which had
demonstrated that in animals, PSK has a **preventive** effect on
chemical carcinogen-induced, radiation-induced, and spontaneously
developed carcinogenesis (Kobayashi et al., *Cancer Epidemiol.,
Biomarkers and Prev.*, 2: 271-276, 1993). We now focus on the effects of
PSK once the progression of carcinogenesis has begun, and review what
is now known of the **preventive** action of PSK on **cancer**
metastasis.

Recent research reports that PSK suppresses pulmonary metastasis of
methylcholanthrene-induced sarcomas, human prostate **cancer**
DU145M, and lymphatic metastasis of mouse leukemia P388, and that it
has prolonged the survival period in spontaneous metastasis models. PSK
also suppresses the metastasis of rat hepatoma AH60C, mouse colon
cancer colon 26, and mouse leukemia BL male 1 in artificial
metastasis models.

PSK influences the steps of **cancer** metastasis in a number of
ways: (a) by suppression of intravasation through the inhibition of
tumor invasion, adhesion and production of cell matrix-degrading
enzymes; (b) by suppression of **tumor** cell attachment to
endothelial cells through the inhibition of **tumor** cert-induced
platelet aggregation; (c) by suppression of **tumor** cell migration
after extravasation through the inhibition of **tumor** cell
motility; and (d) by suppression of **tumor** growth after
extravasation through the inhibition of angiogenesis, the modulation of

cytokine production, and the augmentation of effector cell functions. In addition, PSK has suppressed the **malignant** progression of mouse **tumor** cells through superoxide trapping.

It therefore seems that PSK suppresses **cancer** metastasis at any number of different steps rather than at one particular step, and that its primary action mechanism can be ascribed to direct action on the **tumor** cell as well as to immunomodulation. Since PSK has few side effects and can be administered p.o. over long periods of time, it appears to be a useful agent for controlling or **preventing cancer** metastasis.

, 1995

...Abstract: We have previously reviewed recent research which had demonstrated that in animals, PSK has a **preventive** effect on chemical carcinogen-induced, radiation-induced, and spontaneously developed carcinogenesis (Kobayashi et al., **Cancer Epidemiol., Biomarkers and Prev.**, 2: 271-276, 1993). We now focus on the effects of ...

...once the progression of carcinogenesis has begun, and review what is now known of the **preventive** action of PSK on **cancer** metastasis.

Recent research reports that PSK suppresses pulmonary metastasis of methylcholanthrene-induced sarcomas, human prostate **cancer** DU145M, and lymphatic metastasis of mouse leukemia P388, and that it has prolonged the survival...

...in spontaneous metastasis models. PSK also suppresses the metastasis of rat hepatoma AH60C, mouse colon **cancer** colon 26, and mouse leukemia BL male 1 in artificial metastasis models.

PSK influences the steps of **cancer** metastasis in a number of ways: (a) by suppression of intravasation through the inhibition of **tumor** invasion, adhesion and production of cell matrix-degrading enzymes; (b) by suppression of **tumor** cell attachment to endothelial cells through the inhibition of **tumor** cert-induced platelet aggregation; (c) by suppression of **tumor** cell migration after extravasation through the inhibition of **tumor** cell motility; and (d) by suppression of **tumor** growth after extravasation through the inhibition of angiogenesis, the modulation of cytokine production, and the augmentation of effector cell functions. In addition, PSK has suppressed the **malignant** progression of mouse **tumor** cells through superoxide trapping.

It therefore seems that PSK suppresses **cancer** metastasis at any number of different steps rather than at one particular step, and that its primary action mechanism can be ascribed to direct action on the **tumor** cell as well as to immunomodulation. Since PSK has few side effects and can be...

...over long periods of time, it appears to be a useful agent for controlling or **preventing cancer** metastasis.

...Identifiers--3-METHYLCHOLANTHRENE-INDUCED AUTOCHTHONOUS TUMORS; **ACTIVATED** KILLER-CELLS; COLORECTAL-**CANCER**; BLOOD-LYMPHOCYTES; **SURGICAL** REMOVAL; C57BL/6 MICE; IMMUNOMODULATOR; ADENOCARCINOMA; INTERFERON; **CARCINOMA**

15/3,K,AB/29 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

03017240 Genuine Article#: MW615 Number of References: 42
Title: INDUCTION BY INTERLEUKIN-7 OF LYMPHOKINE-**ACTIVATED** KILLER
ACTIVITY IN **LYMPHOCYTES** FROM AUTOLOGOUS AND SYNGENEIC MARROW

TRANSPLANT RECIPIENTS BEFORE AND AFTER SYSTEMIC INTERLEUKIN-2 THERAPY
(Abstract Available)

Author(s): PAVLETIC Z; BENYUNES MC; THOMPSON JA; LINDGREN CG; MASSUMOTO C;
ALDERSON MR; BUCKNER CD; FEFER A

Corporate Source: UNIV WASHINGTON, MED CTR, MAILSTOP RM-17, 1959 NE PACIFIC
ST/SEATTLE//WA/98195; FRED HUTCHINSON CANC RES CTR, DIV CLIN
RES/SEATTLE//WA/98104; UNIV WASHINGTON, SCH MED, DEPT MED, DIV
ONCOL/SEATTLE//WA/98195; IMMUNEX CORP/SEATTLE//WA/00000

Journal: EXPERIMENTAL HEMATOLOGY, 1993, V21, N10 (SEP), P1371-1378

ISSN: 0301-472X

Language: ENGLISH Document Type: ARTICLE

Abstract: Therapy with recombinant lymphokines after autologous bone marrow transplantation (ABMT) is being explored as a way to **prevent** relapse. Lymphokine therapy may exert an antitumor effect through a variety of mechanisms, including the induction of lymphokine-activated killer (LAK) cell cytotoxicity. We tested the ability of interleukin-7 (IL-7) to induce LAK cytotoxicity in peripheral blood mononuclear cells (PBMC) from healthy subjects and from patients early after ABMT. LAK activity was defined as lysis of Daudi by PBMC after incubation with IL-7 at 10 to 100 ng/mL or IL-2 at 1000 U/mL. PBMC from four healthy subjects were cultured with either IL-7 or IL-2. IL-7 induced LAK activity in two of the four, whereas IL-2 induced LAK activity in all four. The median percent lysis (effector-to-target ratio [E:T] 40:1) with IL-7 (23%) was lower than with IL-2 (67%). PBMC were obtained from 15 patients 27 to 84 days after autologous (n=13) or syngeneic (n=2) bone marrow transplantation (BMT) and tested for IL-7-induced LAK activity. Eleven exhibited significant activity (10% to 77% lysis at E:T 40:1). In contrast to the results in PBMC from normal subjects, in PBMC from ABMT patients IL-7 induced LAK activity of a magnitude similar to that induced by IL-2. Studies were also performed on PBMC from eight patients who had received IL-2 after ABMT (3.0x10⁶ U/m²/d) for 4 days by continuous intravenous (IV) infusion. In seven of the eight patients, IL-7 induced significant LAK activity, which was higher than that seen in PBMC from ABMT patients who had not received IL-2. Thus, IL-7 reproducibly induced significant LAK activity in cells obtained early after autologous or syngeneic BMT. Indeed, such LAK activity was comparable quantitatively to that induced by IL-2. Finally, IL-7 induced an even greater LAK activity in vitro in PBMC obtained after ABMT and preactivated in vivo by IL-2 therapy. The results suggest that IL-7 may have a potential immunotherapeutic role, alone or with IL-2, after ABMT.

Title: INDUCTION BY INTERLEUKIN-7 OF LYMPHOKINE-ACTIVATED KILLER
ACTIVITY IN LYMPHOCYTES FROM AUTOLOGOUS AND SYNGENEIC MARROW
TRANSPLANT RECIPIENTS BEFORE AND AFTER SYSTEMIC INTERLEUKIN-2 THERAPY
, 1993

...Abstract: recombinant lymphokines after autologous bone marrow transplantation (ABMT) is being explored as a way to **prevent** relapse. Lymphokine therapy may exert an antitumor effect through a variety of mechanisms, including the...

...Research Fronts: 1191 002 (AUTOLOGOUS BONE-MARROW TRANSPLANTATION;
GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (GM-CSF); HIGH-DOSE
CHEMOTHERAPY)

92-1406 002 (RECOMBINANT INTERLEUKIN-2 IN METASTATIC RENAL-CELL
CARCINOMA; ADOPTIVE IMMUNOTHERAPY OF CANCER; TUMOR
INFILTRATING LYMPHOCYTES)

92-4826 001 (BONE-MARROW STROMAL CELLS; LONG-TERM HEMATOPOIETIC
CULTURES; INVITRO GROWTH...)

15/3,K,AB/30 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

02054756 Genuine Article#: JX169 Number of References: 21
Title: **PREVENTION OF MYELOSUPPRESSION DOES NOT IMPROVE THE
THERAPEUTIC EFFICACY OF CHEMOIMMUNOTHERAPY** (Abstract Available)
Author(s): LUMSDEN AJ; CODDE JP; GRAY BN; VANDERMEIDE PH
Corporate Source: UNIV PERTH, ROYAL PERTH HOSP, DEPT SURG/PERTH
6000//AUSTRALIA/; TNO, INST APPL RADIOBIOL &
IMMUNOL, IMMUNOMODULATSECT/2280 HV RIJSWIJK//NETHERLANDS/
Journal: ANTICANCER RESEARCH, 1992, V12, N5 (SEP-OCT), P1725-1729
ISSN: 0250-7005

Language: ENGLISH Document Type: ARTICLE

Abstract: This study was designed to investigate whether the **prevention** of doxorubicin (DOX) induced myelosuppression could further improve the therapeutic efficacy of chemoimmunotherapy with DOX, interleukin-2 (IL-2) and interferon gamma (IFN-gamma). The antitumour activity of systemic IL-2/IFN-gamma immunotherapy in combination with DOX administered either systemically, regionally or on ion-exchange microspheres, was assessed in WAG rats bearing hind limb solid colonic adenocarcinoma implants. Whilst the use of microspheres to transport DOX clearly avoided the myelosuppression, systemic and renal toxicity associated with the use of free DOX, it did not provide any therapeutic advantage over chemo-immunotherapy with free systemic or regional drug.

Title: **PREVENTION OF MYELOSUPPRESSION DOES NOT IMPROVE THE
THERAPEUTIC EFFICACY OF CHEMOIMMUNOTHERAPY**
, 1992

Abstract: This study was designed to investigate whether the **prevention** of doxorubicin (DOX) induced myelosuppression could further improve the therapeutic efficacy of chemoimmunotherapy with DOX
...

...Identifiers--**TUMOR-INFILTRATING LYMPHOCYTES; RECOMBINANT
INTERLEUKIN-2; ADRIAMYCIN; CELLS; TOXICITY; RAT; CHEMOTHERAPY;
MICROSPHERES; INTERFERON; RELEASE**

Research Fronts: 90-0093 001 (RECOMBINANT INTERLEUKIN-2; LYMPHOKINE-
**ACTIVATED KILLER-CELLS; TUMOR-INFILTRATING
LYMPHOCYTES; CANCER-PATIENTS RECEIVING ADOPTIVE
IMMUNOTHERAPY**)

15/3,K,AB/31 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

02015353 Genuine Article#: JU458 Number of References: 27
Title: PERIOPERATIVE IMMUNOTHERAPY WITH RECOMBINANT INTERLEUKIN-2 IN
PATIENTS UNDERGOING **SURGERY FOR COLORECTAL-CANCER** (
Abstract Available)

Author(s): NICHOLS PH; RAMSDEN CW; WARD U; SEDMAN PC; PRIMROSE JN
Corporate Source: ST JAMES UNIV HOSP, ACAD UNIT SURG, CLIN SCI BLDG, BECKETT
ST/LEEDS LS9 7TF/W YORKSHIRE/ENGLAND/; ST JAMES UNIV HOSP, ACAD UNIT
SURG, CLIN SCI BLDG, BECKETT ST/LEEDS LS9 7TF/W YORKSHIRE/ENGLAND/

Journal: CANCER RESEARCH, 1992, V52, N20 (OCT 15), P5765-5769
ISSN: 0008-5472

Language: ENGLISH Document Type: ARTICLE

Abstract: Major **surgery** impairs the cellular immune response. We have therefore studied the immunological effects of low-dose recombinant interleukin 2 given to patients undergoing **surgery** for colorectal **cancer** to determine whether this agent has potential in perioperative adjuvant immunotherapy. Patients were randomly allocated to control (n = 13) or treatment groups (n = 12). Immunological studies of both lymphocyte function and subset number were performed preoperatively and on Days 1, 4, 7, and 10. Treatment with recombinant interleukin 2 **prevented** the postoperative fall in both natural killer and lymphokine-activated killer cell cytotoxicity, clearly

demonstrated in the control group. The treatment group also showed in vivo T-cell activation with an initial lymphopenia followed by a rebound lymphocytosis and upregulation of the subset markers CD25 (interleukin 2 receptor) and CD45RO (T-memory cells). These combined effects may have important consequences in controlling metastatic dissemination of **tumor** during the vulnerable perioperative period.

Title: PERIOPERATIVE IMMUNOTHERAPY WITH RECOMBINANT INTERLEUKIN-2 IN PATIENTS UNDERGOING **SURGERY** FOR COLORECTAL-**CANCER**, 1992

Abstract: Major **surgery** impairs the cellular immune response. We have therefore studied the immunological effects of low-dose recombinant interleukin 2 given to patients undergoing **surgery** for colorectal **cancer** to determine whether this agent has potential in perioperative adjuvant immunotherapy. Patients were randomly allocated ...

...performed preoperatively and on Days 1, 4, 7, and 10. Treatment with recombinant interleukin 2 **prevented** the postoperative fall in both natural killer and lymphokine-activated killer cell cytotoxicity, clearly demonstrated...

...T-memory cells). These combined effects may have important consequences in controlling metastatic dissemination of **tumor** during the vulnerable perioperative period.

...Identifiers--KILLER CELLS; LYMPHOCYTES; LEVAMISOLE; INTERFERON; OPERATIONS; METASTASES; **CARCINOMA**; RESPONSES; THERAPY; TRIAL

Research Fronts: 90-0093 004 (RECOMBINANT INTERLEUKIN-2; LYMPHOKINE-ACTIVATED KILLER-CELLS; **TUMOR**-INFILTRATING LYMPHOCYTES; **CANCER**-PATIENTS RECEIVING ADOPTIVE IMMUNOTHERAPY)

90-3602 001 (ADJUVANT THERAPY; COLON **CANCER**; PORTAL-VEIN **CHEMOTHERAPY**)

? log off

25feb03 12:30:49 User231882 Session D1142.3

\$8.05 2.516 DialUnits File155

\$2.31 11 Type(s) in Format 4 (UDF)

\$2.31 11 Types

\$10.36 Estimated cost File155

\$8.28 1.479 DialUnits File55

\$10.50 6 Type(s) in Format 4 (UDF)

\$10.50 6 Types

\$18.78 Estimated cost File55

\$54.26 2.933 DialUnits File34

\$74.90 14 Type(s) in Format 55 (UDF)

\$74.90 14 Types

\$129.16 Estimated cost File34

\$11.56 0.625 DialUnits File434

\$11.56 Estimated cost File434

\$23.29 1.479 DialUnits File340

\$23.29 Estimated cost File340

OneSearch, 5 files, 9.031 DialUnits FileOS

\$3.50 TELNET

\$196.65 Estimated cost this search

\$196.71 Estimated total session cost 9.249 DialUnits

Logoff: level 02.12.60 D 12:30:49

? ds

Set	Items	Description
S1	39262	PREVENT? (5N) (CANCER OR TUMOR OR CARCINOMA OR MALIGNAN?)
S2	678612	LYMPHOCYTE??
S3	1558	S1 AND S2
S4	157862	CD(W)3 OR CD3 OR OKT3 OR OKT(W)3 OR INTERLEUKIN(W)2
S5	283	S3 AND S4
S6	250	S5 AND PY<=2001
S7	2121826	YEAR??
S8	7	S6 AND S7
S9	7	RD (unique items)

? s primed

S10	37288	PRIMED
-----	-------	--------

? s s3 and s10

	1558	S3
	37288	S10
S11	33	S3 AND S10

? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.

...completed examining records

S12	22	RD (unique items)
-----	----	-------------------

? s s12 and py<=2001

Processing

Processing

	22	S12
	40185934	PY<=2001
S13	19	S12 AND PY<=2001

? t s13/3,k,ab/1-19

13/3,K,AB/1 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

11035078 20581132 PMID: 11145646

Regulation of the CTL response by macrophage migration inhibitory factor.

Abe R; Peng T; Sailors J; Bucala R; Metz C N

Laboratories of Vascular Biology and Medical Biochemistry, The Picower Institute for Medical Research, Manhasset, NY 11030, USA.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Jan 15 2001, 166 (2) p747-53, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Macrophage migration inhibitory factor (MIF) has been shown to be a pivotal cytokine that mediates host inflammatory and immune responses. Recently, immunoneutralization of MIF has been found to inhibit tumor growth in mice; however, the contributing mechanisms underlying this effect have not been well defined. We investigated whether MIF plays a regulatory role in the expression of CTL activity. In a mouse model of the CTL response using the OVA-transfected tumor cell line EL4 (EG.7), we found that cultures of splenocytes obtained from EG.7-**primed** mice secrete high levels of MIF following Ag stimulation in vitro. Notably, parallel splenocyte cultures treated with neutralizing anti-MIF mAb showed a significant increase in the CTL response directed against EG.7 cells compared with control mAb-treated cultures. This effect was accompanied by elevated expression of IFN-gamma. Histological examination of the EG.7 tumors from anti-MIF-treated animals showed a prominent increase in both CD4(+) and CD8(+) T cells as well as apoptotic tumor cells, consistent with the observed augmentation of CTL activity in vivo by anti-MIF. This increased CTL activity was associated with enhanced expression of the

common gamma(c)-chain of the IL-2R that mediates CD8(+) T cell survival. Finally, CD8(+) T **lymphocytes** obtained from the spleens of anti-MIF-treated EG.7 tumor-bearing mice, when transferred into recipient tumor-bearing mice, showed increased accumulation in the tumor tissue. These data provide the first evidence of an important role for MIF in the regulation and trafficking of anti-tumor T **lymphocytes** in vivo.

Jan 15 2001,

... cell line EL4 (EG.7), we found that cultures of splenocytes obtained from EG.7-**primed** mice secrete high levels of MIF following Ag stimulation in vitro. Notably, parallel splenocyte cultures...

... c)-chain of the IL-2R that mediates CD8(+) T cell survival. Finally, CD8(+) T **lymphocytes** obtained from the spleens of anti-MIF-treated EG.7 tumor-bearing mice, when transferred...

... of an important role for MIF in the regulation and trafficking of anti-tumor T **lymphocytes** in vivo.

Descriptors: Cytotoxicity, Immunologic--immunology--IM; *Macrophage Migration-Inhibitory Factors--physiology--PH; *T-**Lymphocytes**, Cytotoxic--immunology--IM...; and dosage--AD; Antibodies, Monoclonal--pharmacology--PD; Antibodies, Monoclonal--therapeutic use--TU; CD8-Positive T-**Lymphocytes**--immunology--IM; Cell Movement--immunology--IM; Cells, Cultured; Cytotoxicity Tests, Immunologic; Injections, Intraperitoneal; **Lymphocytes**, Tumor-Infiltrating--immunology--IM; Macrophage Migration-Inhibitory Factors--immunology--IM; Mice; Mice, Inbred C57BL; Neoplasm Transplantation; Thymoma--immunology--IM; Thymoma--pathology--PA; Thymoma--**prevention** and control--PC; **Tumor** Cells, Cultured--transplantation--TR

13/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10722262 20273972 PMID: 10811859

Human CD4(+) T **lymphocytes** consistently respond to the latent Epstein-Barr virus nuclear antigen EBNA1.

Munz C; Bickham K L; Subklewe M; Tsang M L; Chahroudi A; Kurilla M G; Zhang D; O'Donnell M; Steinman R M

Laboratory of Cellular Physiology and Immunology, The Rockefeller University, New York, New York 10021-6399, USA.

Journal of experimental medicine (UNITED STATES) May 15 2000,

191 (10) p1649-60, ISSN 0022-1007 Journal Code: 2985109R

Contract/Grant No.: AZ40874; PHS; K12-HD00850; HD; NICHD

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The Epstein-Barr virus (EBV)-encoded nuclear antigen EBNA1 is critical for the persistence of the viral episome in replicating EBV-transformed human B cells. Therefore, all EBV-induced tumors express this foreign antigen. However, EBNA1 is invisible to CD8(+) cytotoxic T **lymphocytes** because its Gly/Ala repeat domain prevents proteasome-dependent processing for presentation on major histocompatibility complex (MHC) class I. We now describe that CD4(+) T cells from healthy adults are **primed** to EBNA1. In fact, among latent EBV antigens that stimulate CD4(+) T cells, EBNA1 is preferentially recognized. We present evidence that the CD4(+) response may provide a protective role, including interferon gamma secretion and direct cytolysis after encounter of transformed B **lymphocyte** cell lines (B-LCLs). Dendritic cells (DCs) process EBNA1 from purified protein and from MHC class II-mismatched, EBNA1-expressing cells including B-LCLs. In contrast, B-LCLs and Burkitt's lymphoma lines likely present EBNA1 after endogenous processing, as their capacity to cross-present from exogenous sources is

weak or undetectable. By limiting dilution, there is a tight correlation between the capacity of CD4(+) T cell lines to recognize autologous B-LCL-expressing EBNA1 and DCs that have captured EBNA1. Therefore, CD4(+) T cells can respond to the EBNA1 protein that is crucial for EBV persistence. We suggest that this immune response is initiated in vivo by DCs that present EBV-infected B cells, and that EBNA1-specific CD4(+) T cell immunity be enhanced to **prevent** and treat EBV-associated **malignancies**.

Human CD4(+) T **lymphocytes** consistently respond to the latent Epstein-Barr virus nuclear antigen EBNA1.

May 15 2000,

... EBV-induced tumors express this foreign antigen. However, EBNA1 is invisible to CD8(+) cytotoxic T **lymphocytes** because its Gly/Ala repeat domain prevents proteasome-dependent processing for presentation on major histocompatibility complex (MHC) class I. We now describe that CD4(+) T cells from healthy adults are **primed** to EBNA1. In fact, among latent EBV antigens that stimulate CD4(+) T cells, EBNA1 is...

... a protective role, including interferon gamma secretion and direct cytolysis after encounter of transformed B **lymphocyte** cell lines (B-LCLs). Dendritic cells (DCs) process EBNA1 from purified protein and from MHC...

... EBV-infected B cells, and that EBNA1-specific CD4(+) T cell immunity be enhanced to **prevent** and treat EBV-associated **malignancies**.

Descriptors: CD4-Positive T-**Lymphocytes**--immunology--IM; *Epstein-Barr Virus Nuclear Antigens--immunology--IM; Adult; Antigen Presentation; B-**Lymphocytes**--immunology--IM; Cell Line; Dendritic Cells--immunology--IM; Epitopes--chemistry--CH; Epitopes--genetics--GE; Epstein...

...Herpesvirus 4, Human--genetics--GE; Herpesvirus 4, Human--immunology--IM; Interferon Type II--biosynthesis--BI; **Lymphocyte** Transformation; Protein Structure, Tertiary; Repetitive Sequences, Amino Acid

13/3,K,AB/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

10431764 99421815 PMID: 10490962

T cell memory against colon carcinoma is long-lived in the absence of antigen.

Xiang R; Lode H N; Gillies S D; Reisfeld R A

Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037; USA.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Oct 1 1999, 163 (7) p3676-83, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: 1R35CA42508; CA; NCI; 2U19CA37641; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Eradication of established colon carcinoma metastases is a major goal for adjuvant immunotherapy of this disease. This was accomplished in a murine model by targeting IL-2 to the tumor microenvironment with a recombinant Ab-IL-2 fusion protein (huKS1/4-IL-2). The generation of a long-lived protective immunity was demonstrated by a 10- to 14-fold increase in CTL precursor (pCTL) frequency and induction of genes encoding Th1 cytokines, followed by the generation of tumor-specific CD8+ T effector cells, some of which differentiated into long-lived T memory cells. The frequency of pCTL correlated with enhanced immune protection against tumor cell challenge, and long-lived T cell memory was maintained in syngeneic SCID mice in the absence of tumor Ag. Tumor cell challenge of these SCID mice, concomitant

with a boost of two noncurative doses of huKS1/4-IL-2 fusion protein, resulted in the generation of **primed** CD8+ T effector cells with concurrent release of Th1 cytokines. These events culminated in the complete rejection of the **tumor** cell challenge and **prevention** of pulmonary metastases. Taken together, the data suggest that T cell memory against colon carcinoma can be maintained in the absence of Ag.

Oct 1 1999,

... two noncurative doses of huKS1/4-IL-2 fusion protein, resulted in the generation of **primed** CD8+ T effector cells with concurrent release of Th1 cytokines. These events culminated in the complete rejection of the **tumor** cell challenge and **prevention** of pulmonary metastases. Taken together, the data suggest that T cell memory against colon carcinoma

...
Descriptors: Antigens, Neoplasm--genetics--GE; *Colonic Neoplasms--immunology--IM; *Immunologic Memory; *T-Lymphocytes--immunology--IM; Antigens, Neoplasm--administration and dosage--AD; CD8-Positive T-Lymphocytes--immunology--IM; CD8-Positive T-Lymphocytes--transplantation--TR; Cell Differentiation--genetics--GE; Cell Differentiation--immunology--IM; Chimeric Proteins--administration and dosage...

...Gene Expression Regulation--immunology--IM; Interleukin-2--administration and dosage--AD; Interleukin-2--genetics--GE; Lymphocyte Count; Lymphocyte Transformation--genetics--GE; Mice; Mice, Inbred BALB C; Mice, SCID; Stem Cells--immunology--IM; T-Lymphocytes, Cytotoxic--immunology--IM; Th1 Cells--metabolism--ME; Time Factors; Tumor Cells, Cultured--transplantation--TR

13/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10333871 99321245 PMID: 10395322

CD40 activation in vivo overcomes peptide-induced peripheral cytotoxic T-lymphocyte tolerance and augments anti-tumor vaccine efficacy.

Diehl L; den Boer A T; Schoenberger S P; van der Voort E I; Schumacher T N; Melief C J; Offringa R; Toes R E

Department of Immunohematology and Bloodbank, Leiden University Medical Center, The Netherlands.

Nature medicine (UNITED STATES) Jul 1999, 5 (7) p774-9, ISSN 1078-8956 Journal Code: 9502015

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The outcome of antigen recognition by naive CD8+ cytotoxic T lymphocytes (CTLs) in the periphery is orchestrated by CD4+ T-helper cells, and can either lead to priming or tolerization. The presence of T-helper cells favors the induction of CTL immunity, whereas the absence of T-helper cells can result in CTL tolerance. The action of T helper cells in CTL priming is mediated by CD40-CD40 ligand interactions. We demonstrate here that triggering of CD40 in vivo can considerably enhance the efficacy of peptide-based anti-tumor vaccines. The combination of a tolerogenic peptide vaccine containing a minimal essential CTL epitope with an activating antibody against CD40 converts tolerization into strong CTL priming. Moreover, CD40 ligation can provide an already protective tumor-specific peptide vaccine with the capacity to induce therapeutic CTL immunity in tumor-bearing mice. These findings indicate that the CD40-CD40 ligand pair can act as a 'switch', determining whether naive peripheral CTLs are **primed** or tolerized, and support the clinical use of CD40-stimulating agents as components of anti-cancer vaccines.

CD40 activation in vivo overcomes peptide-induced peripheral cytotoxic T-**lymphocyte** tolerance and augments anti-tumor vaccine efficacy.

Jul 1999,

The outcome of antigen recognition by naive CD8+ cytotoxic T **lymphocytes** (CTLs) in the periphery is orchestrated by CD4+ T-helper cells, and can either lead...

... CD40-CD40 ligand pair can act as a 'switch', determining whether naive peripheral CTLs are **primed** or tolerized, and support the clinical use of CD40-stimulating agents as components of anti...

Descriptors: Adenovirus E1A Proteins--immunology--IM; *Antigens, CD40 --physiology--PH; *B-**Lymphocytes**--immunology--IM; ***Cancer** Vaccines; *Neoplasms, Experimental--**prevention** and control--PC; *T-**Lymphocytes**, Cytotoxic--immunology--IM; *T-**Lymphocytes** , Helper-Inducer--immunology--IM; Antigens, CD40--genetics--GE; CD40 Ligand; Cell Transformation, Neoplastic; Epitopes--immunology--IM; Immune Tolerance ; **Lymphocyte** Transformation; Membrane Glycoproteins--physiology--PH; Mice; Mice, Inbred C57BL; Mice, Knockout; Neoplasms, Experimental --immunology--IM...

13/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

10056327 99010930 PMID: 9796906

Induction of tumor-specific T cell response by cognating tumor cells with foreign antigen-**primed** Th cells.

Cheng T Y; Wu J T; Lin R H

Graduate Institute of Microbiology, College of Medicine, National Taiwan University, Taipei, ROC.

International immunology (ENGLAND) Oct 1998, 10 (10) p1397-406

, ISSN 0953-8178 Journal Code: 8916182

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Sufficient CD4+ T cell help is very important in generating specific cytotoxic T cell responses. The inadequate activation of tumor-specific Th cells leads to failure of antitumor immunity. In general, each individual consists of some **primed** Th cells responding to certain antigens. If these tumor non-specific pre-**primed** Th cells can provide sufficient help, the generation of tumor-specific T cells may be enhanced. In the present study, we tested this hypothesis by cognating and reactivating pre-**primed** ovalbumin (OVA)-specific Th cells with OVA-pulsed tumor cells which could simultaneously present both OVA and tumor-associated antigen on the same cell. We clearly demonstrated that immunization of OVA-sensitized mice with OVA-pulsed P388 cells, but not unpulsed P388 cells, led to the induction of P388-specific cytotoxicity and tumor resistance. Both CD4+ and CD8+ tumor-specific cytotoxic T cells were detected in vitro, but only CD8+ T cells played the major effector role in **preventing** the growth of challenged **tumor** in vivo. Taken together, our study demonstrated that the immunogenicity of tumor cells can be enhanced effectively by cognating pre-**primed** foreign antigen-specific Th cells with tumor cells. These findings have potential implications in developing methods to control tumor growth.

Induction of tumor-specific T cell response by cognating tumor cells with foreign antigen-**primed** Th cells.

Oct 1998,

... Th cells leads to failure of antitumor immunity. In general, each individual consists of some **primed** Th cells responding to certain antigens. If these tumor non-specific pre-**primed** Th cells can provide sufficient help, the generation of tumor-specific T cells may be enhanced.

In the present study, we tested this hypothesis by cognating and reactivating pre-primed ovalbumin (OVA)-specific Th cells with OVA-pulsed tumor cells which could simultaneously present both... were detected in vitro, but only CD8+ T cells played the major effector role in preventing the growth of challenged tumor in vivo. Taken together, our study demonstrated that the immunogenicity of tumor cells can be enhanced effectively by cognating pre-primed foreign antigen-specific Th cells with tumor cells. These findings have potential implications in developing...

Descriptors: Antibodies, Neoplasm--immunology--IM; *Antigen Presentation--immunology--IM; *Antigens--immunology--IM; *T-Lymphocytes, Cytotoxic--immunology--IM; *T-Lymphocytes, Helper-Inducer--immunology--IM; Antigens, Neoplasm--immunology--IM; CD4-Positive T-Lymphocytes--immunology--IM; CD8-Positive T-Lymphocytes--immunology--IM; Cell Division--immunology--IM; Freund's Adjuvant--immunology--IM; Immunity, Cellular; Mice; Mice, Inbred DBA; Ovalbumin--immunology--IM; T-Lymphocyte Subsets--immunology--IM; Tumor Cells, Cultured--cytology--CY; Tumor Cells, Cultured--immunology--IM; Tumor Cells...

13/3,K,AB/6 (Item 6 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

09524718 97431155 PMID: 9285248

Study on the mechanism of immunopotentiating antitumor effect of 6-MPG, a water-soluble derivative of 6-mercaptopurine.

Kashida T; Narasaki N; Sakai A; Tsujihara K; Tsuzurahara K; Naito K; Takeyama S

Research Laboratories, Tanabe Seiyaku Co. Ltd., Saitama, Japan.

Immunopharmacology (NETHERLANDS) Aug 1997, 37 (1) p95-104,

ISSN 0162-3109 Journal Code: 7902474

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We investigated possible mechanisms of the antitumor action of gamma-(9H-purine-6-yl) thiomethyl L-glutamate (6-MPG), a water-soluble derivative of 6-MP. In the double grafted tumor system, BALB/c mice were inoculated intradermally with 10(6) cells of MethA fibrosarcoma at the right inguinal region on day 0 (the primary tumor) and later with 3 x 10(6) cells at the left on day 10 (the secondary tumor). Intraperitoneal administration of 6-MPG at a dose of 100 mg/kg/day from day 3 through 7 completely prevented growth of the secondary tumor. 6-MPG showed no effect on growth of colon 26 adenocarcinoma cells inoculated in place of the secondary MethA cells (antigen specificity). 6-MPG did not inhibit the secondary MethA growth in the BALB/c (nu/nu) mouse. The inhibitory effect of 6-MPG on the secondary tumor growth was diminished by prior treatment of the primed animals with cyclosporin A and anti-Thy antibody. Spleen cells from the tumor-bearing mice treated with 6-MPG showed a tumor-neutralizing activity (Winn assay). Treatment of the spleen cells with anti-CD8 antibody plus complement diminished the tumor-neutralizing effect but that with anti-CD4 antibody plus complement did not, indicating that CD8-positive cells are responsible for potentiation of the tumor immunity. These results suggest that the antitumor effect of 6-MPG against the secondary tumor is elicited by augmenting tumor specific T-cell production.

Aug 1997,

...MPG at a dose of 100 mg/kg/day from day 3 through 7 completely prevented growth of the secondary tumor. 6-MPG showed no effect on growth of colon 26 adenocarcinoma cells inoculated in place...

...of 6-MPG on the secondary tumor growth was diminished by prior treatment

of the **primed** animals with cyclosporin A and anti-Thy antibody.
Spleen cells from the tumor-bearing mice...

...; Neoplasm Transplantation; Phenotype; Solubility; Spleen--cytology
--CY; Spleen--drug effects--DE; Spleen--immunology--IM; T-
Lymphocytes--drug effects--DE; T-**Lymphocytes**--immunology--IM;
Water

13/3,K,AB/7 (Item 7 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

09351984 97256579 PMID: 9103420

A tumor-associated and self antigen peptide presented by dendritic cells may induce T cell anergy in vivo, but IL-12 can prevent or revert the anergic state.

Grohmann U; Bianchi R; Ayroldi E; Belladonna M L; Surace D; Fioretti M C; Puccetti P

Department of Experimental Medicine, University of Perugia, Italy.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Apr 15
1997, 158 (8) p3593-602, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Ag-specific CD8+ cell responses, including delayed-type hypersensitivity in vivo and IFN-gamma production in vitro, are initiated by host immunization with P815AB, a self peptide bearing CTL epitopes and expressed by murine mastocytoma cells. Using P815AB-pulsed dendritic cells (DC) and monitoring class I-restricted skin test reactivity in DC-**primed** mice, we have previously shown that the development of a Th1-like response to P815AB requires T helper effects, such as those mediated by coimmunization with class II-restricted (helper) peptides or by the use of rIL-12. The adjuvanticity of IL-12 was suggested to involve improved recognition of class II-restricted epitopes of P815AB. In the present study, we provide evidence for the occurrence of I-A(d)-restricted epitopes in the tumor peptide. We also show that in the absence of helper peptide or rIL-12, P815AB not only failed to initiate CD8+ cell responses in vivo and in vitro, but resulted in a transient state of functional unresponsiveness, characterized by a profound inability of CD4+ cells to produce IL-2 in vitro. Ag-specific T cell anergy was also observed after neutralization of endogenous IL-12 at the time of priming with P815AB plus helper peptide. All of these effects were reversed by rIL-12, which was added to DC cultures and administered to the DC-recipient mice. Anergy induction may thus contribute to P81 5AB unresponsiveness in vivo. IL-12 may act to **prevent** or revert anergy to this **tumor**-associated and self peptide.

Apr 15 1997,

... P815AB-pulsed dendritic cells (DC) and monitoring class I-restricted skin test reactivity in DC-**primed** mice, we have previously shown that the development of a Th1-like response to P815AB...

...induction may thus contribute to P81 5AB unresponsiveness in vivo. IL-12 may act to **prevent** or revert anergy to this **tumor**-associated and self peptide.

Descriptors: Antigen Presentation; *Antigens, Neoplasm--immunology--IM;
*CD8-Positive T-**Lymphocytes**--immunology--IM; *Dendritic Cells
--immunology--IM; *Interleukin-12--immunology--IM

13/3,K,AB/8 (Item 8 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

09106817 97002038 PMID: 8845030

Synthesis of cytokines during tumour development in mice immunized with the mycobacterial antigen complex A60.

Maes H; Cocito C

Medical School University of Louvain, Brussels, Belgium.

Scandinavian journal of immunology (ENGLAND) Oct 1996, 44 (4)
p369-74, ISSN 0300-9475 Journal Code: 0323767

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The authors have previously reported on the ability of A60, an immunodominant antigenic complex of Mycobacterium bovis BCG, to **prevent cancer** development in mice challenged with EMT 6 tumour cells. Such effect proved to rely on neoplastic cell lysis by cytolytic T **lymphocytes** and activated macrophages. The involvement of cytokines in triggering the immune response leading to tumour rejection is analysed in the present work. The synthesis of IL-2, IFN-gamma and TNF-alpha was strongly increased in A60-**primed** mice. Cancer development depressed the blood levels of these three cytokines. In vitro cultures of **lymphocytes** from lymph nodes and blood of A60-**primed** mice produced higher levels of these cytokines in the presence of A60, as compared to cultures lacking A60. Such effect was inhibited by co-incubation of **lymphocytes** with EMT 6 tumour cells. In vitro cultures of macrophages yielded higher levels of TNF-alpha in the presence of A60 and co-incubation of these cells with EMT 6 tumour cells also inhibited TNF-alpha production. The enhanced synthesis of IL-2 and IFN-gamma, which promote activation of cytolytic T **lymphocytes** and macrophages, accounts for the increased tumour cell lysis induced in vivo by A60. The A60-promoted synthesis of TNF-alpha is partly responsible for the latter effect. The inhibitory action of EMT-6 tumour cells on cytokine synthesis is a powerful mechanism of tumour escape from the immune system's control.

Oct 1996,

...reported on the ability of A60, an immunodominant antigenic complex of Mycobacterium bovis BCG, to **prevent cancer** development in mice challenged with EMT 6 tumour cells. Such effect proved to rely on neoplastic cell lysis by cytolytic T **lymphocytes** and activated macrophages. The involvement of cytokines in triggering the immune response leading to tumour...

...The synthesis of IL-2, IFN-gamma and TNF-alpha was strongly increased in A60-**primed** mice. Cancer development depressed the blood levels of these three cytokines. In vitro cultures of **lymphocytes** from lymph nodes and blood of A60-**primed** mice produced higher levels of these cytokines in the presence of A60, as compared to cultures lacking A60. Such effect was inhibited by co-incubation of **lymphocytes** with EMT 6 tumour cells. In vitro cultures of macrophages yielded higher levels of TNF...

... The enhanced synthesis of IL-2 and IFN-gamma, which promote activation of cytolytic T **lymphocytes** and macrophages, accounts for the increased tumour cell lysis induced in vivo by A60. The...

; Cells, Cultured; Cytokines--blood--BL; Interleukin-2--biosynthesis--BI; **Lymphocytes**--metabolism--ME; Mice; Mice, Inbred BALB C; Neoplasm Transplantation; Neoplasms, Experimental--pathology--PA; Tumor Cells...

13/3,K,AB/9 (Item 9 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

09103441 97008936 PMID: 8856046

Gangliosides block antigen presentation by human monocytes.

Heitger A; Ladisch S

Glycobiology Program, Center for Cancer and Transplantation Biology,
Children's Research Institute, Washington, DC 20010, USA.

Biochimica et biophysica acta (NETHERLANDS) Sep 27 1996, 1303

(2) p161-8, ISSN 0006-3002 Journal Code: 0217513

Contract/Grant No.: CA42361; CA; NCI; CA61010; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Gangliosides, immunosuppressive molecules shed by tumor cells, are potent inhibitors of monocyte accessory cell function. However, the specific monocyte cellular defect caused by gangliosides is unknown. Here we sought to delineate whether this abnormality is in the induction of suppressor cells, in intracellular antigen processing, or in intercellular antigen presentation. Three sets of studies of the tetanus toxoid (TT)-induced lymphoproliferative response, which is dependent upon monocyte accessory function, address this issue: (1) Antigen (TT)-**primed** human monocytes incubated with 50-100 microM human brain gangliosides for 24-48 h, washed, and then combined with T-cells, were inhibited in triggering T-cell proliferation, showing that the effect was occurring after antigen processing was complete. (2) T-cell responses to immobilized anti-CD3 or to antigen-**primed** control monocytes in the presence of ganglioside-exposed monocytes were unaffected, showing that ganglioside-exposed monocytes did not act as suppressor cells. (3) Stimulation by TT peptide fragment 830-843, which does not require processing, was completely inhibited by exposure of monocytes to gangliosides. These findings identify ganglioside interference with monocyte accessory cell function at the level of antigen presentation. We conclude that tumor gangliosides may inhibit host anti-**tumor** cellular immune responses by **preventing** the effective cellular interactions of the antigen-**primed** monocyte with the responding T-**lymphocyte**.

Sep 27 1996,

... lymphoproliferative response, which is dependent upon monocyte accessory function, address this issue: (1) Antigen (TT)-**primed** human monocytes incubated with 50-100 microM human brain gangliosides for 24-48 h, washed...

... antigen processing was complete. (2) T-cell responses to immobilized anti-CD3 or to antigen-**primed** control monocytes in the presence of ganglioside-exposed monocytes were unaffected, showing that ganglioside-exposed...

... at the level of antigen presentation. We conclude that tumor gangliosides may inhibit host anti-**tumor** cellular immune responses by **preventing** the effective cellular interactions of the antigen-**primed** monocyte with the responding T-**lymphocyte**.

; Antigens--immunology--IM; Brain Chemistry; Gangliosides--isolation and purification--IP; **Lymphocyte** Transformation--drug effects--DE; Monocytes--immunology--IM; Monocytes--metabolism--ME; Peptide Fragments--immunology--IM; T-**Lymphocyte** Subsets--immunology--IM; Tetanus Toxoid--immunology--IM

13/3,K,AB/10 (Item 10 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

08824218 96179385 PMID: 8602462

Cancer prevention by adoptive transfer of antigen
60-activated immunocompetent cells.

Maes H; Cocito C
Laboratory of Microbiology and Molecular Genetics, Medical School,
University of Louvain, Brussels, Belgium.

Scandinavian journal of immunology (ENGLAND) Mar 1996, 43 (3)
p283-8, ISSN 0300-9475 Journal Code: 0323767

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The authors have already shown that A60, the thermostable macromolecular antigen complex of Mycobacterium bovis BCG, induced resistance to tumour challenge in several murine systems. In the present work, the authors provided evidence that activated macrophages played a major role, and cytolytic T **lymphocytes** a minor one, in both in vivo and in vitro A60-promoted cancer cell cytotoxicity. To identify the types of immunocompetent cells involved in this protective effect, macrophages and T **lymphocytes** from A60-primed mice donors were adoptively transferred to irradiated recipients prior to EMT 6 tumour challenge. In some groups, A60-primed donors were survivors of previous tumour challenges. Transfer of T **lymphocytes** from the spleen or lymph-nodes of A60-immunized mice induced 80-90% protection against tumour challenge. Conversely, transferred macrophages, although cytolytically active, did not induce resistance to tumour implantation. Furthermore, adoptive transfer with T **lymphocytes** from A60-immunized and EMT 6 challenge-surviving donors induced 100% protection. It is concluded that stimulation of T **lymphocytes** by A60 is the key step which leads to activation of the immunocompetent cells involved in tumour rejection.

Cancer prevention by adoptive transfer of antigen
60-activated immunocompetent cells.

Mar 1996,

... work, the authors provided evidence that activated macrophages played a major role, and cytolytic T **lymphocytes** a minor one, in both in vivo and in vitro A60-promoted cancer cell cytotoxicity. To identify the types of immunocompetent cells involved in this protective effect, macrophages and T **lymphocytes** from A60-primed mice donors were adoptively transferred to irradiated recipients prior to EMT 6 tumour challenge. In some groups, A60-primed donors were survivors of previous tumour challenges. Transfer of T **lymphocytes** from the spleen or lymph-nodes of A60-immunized mice induced 80-90% protection against...

... although cytolytically active, did not induce resistance to tumour implantation. Furthermore, adoptive transfer with T **lymphocytes** from A60-immunized and EMT 6 challenge-surviving donors induced 100% protection. It is concluded that stimulation of T **lymphocytes** by A60 is the key step which leads to activation of the immunocompetent cells involved...

Descriptors: Antigens, Bacterial--immunology--IM; *Immunotherapy, Adoptive; ***Lymphocyte** Transformation; *Macrophage Activation; *Macrophages--immunology--IM; *Mammary Neoplasms, Experimental--prevention and control--PC; *T-**Lymphocytes**, Cytotoxic--immunology--IM...; transplantation--TR; Mammary Neoplasms, Experimental--immunology--IM; Mice; Mice, Inbred BALB C; Radiation Chimera; T-**Lymphocytes**, Cytotoxic --transplantation--TR; Tumor Cells, Cultured

13/3,K,AB/11 (Item 11 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

08434093 95194736 PMID: 7888229

Ultraviolet-light-inactivated Cas-Br-M murine leukemia virus induces a protective CD8+ cytotoxic T **lymphocyte** response in newborn mice.

Sarzotti M; Dean T A; Remington M; Hoffman P M

Retrovirus Research Center, Veterans Affairs Medical Center, Baltimore, Maryland 21201.

AIDS research and human retroviruses (UNITED STATES) Dec 1994,
10 (12) p1695-702, ISSN 0889-2229 Journal Code: 8709376
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Newborn NFS/N mice are susceptible to the neurological disease induced by infection with Cas-Br-M murine leukemia virus (Cas), and do not develop a protective cytotoxic T cell (CTL)-mediated response to Cas infection. Here we demonstrate that whole UV light-inactivated Cas (UV-Cas), inoculated in newborn NFS/N mice, induced a strong, Cas-specific CTL response detectable 2 weeks postinoculation and persisting in vivo for > or = 36 weeks. The magnitude of the UV-Cas-induced splenic CTL response, mediated by CD8+ T cells, inversely correlated with the level of proviral cas env sequences detectable in the spleen of the UV-Cas-inoculated mice, as revealed by PCR amplification of tissue DNA. The transfer of UV-Cas-primed splenocytes, with Cas-specific CTL activity, protected 100% of recipient newborn mice from the development of neurological disease induced by infection with live Cas, for more than 28 weeks, and reduced the level of viral replication in the recipients.

Ultraviolet-light-inactivated Cas-Br-M murine leukemia virus induces a protective CD8+ cytotoxic T lymphocyte response in newborn mice.

Dec 1994,

... inoculated mice, as revealed by PCR amplification of tissue DNA. The transfer of UV-Cas-primed splenocytes, with Cas-specific CTL activity, protected 100% of recipient newborn mice from the development...

Descriptors: CD8-Positive T-Lymphocytes--immunology--IM; *Leukemia Virus, Murine--immunology--IM; *Nervous System Diseases--immunology--IM; *Retroviridae Infections--immunology--IM; *T-Lymphocytes, Cytotoxic--immunology--IM; *Viral Vaccines--immunology--IM...; and control--PC; Retroviridae Infections--virology--VI; Spleen--cytology--CY; Tumor Virus Infections--immunology--IM; Tumor Virus Infections--prevention and control--PC; Tumor Virus Infections--virology--VI; Ultraviolet Rays; Vaccines, Inactivated--immunology--IM

13/3,K,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

06773050 91088561 PMID: 2263613

Analysis of interleukin 2 and various effector cell populations in adoptive immunotherapy of 9L rat gliosarcoma: allogeneic cytotoxic T lymphocytes prevent tumor take.

Kruse C A; Lillehei K O; Mitchell D H; Kleinschmidt-DeMasters B; Bellgrau D

Department of Surgery, University of Colorado Health Science Center, Denver 80262.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 1990, 87 (24) p9577-81, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: KO4-NS01401; NS; NINDS; RO1-NS28905; NS; NINDS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Recombinant interleukin 2 (rIL-2) and various effector cell populations were used for adoptive immunotherapy in the Fischer strain 9L rat gliosarcoma model. The in vivo cytotoxicities of nonspecifically activated lymphocytes and specifically activated cytotoxic T lymphocytes (CTLs) were assessed in a modified in vivo neutralization (Winn) assay. Effector cells (10(6)) and 9L tumor cells (10(5)) were combined with 10(4) units of rIL-2 and stereotactically implanted into the right frontal

centrum semiovale of the Fischer (F344) rat. At 7 and 14 days, additional effector cells (10(6) and rIL-2 (10(4) units) were administered through the same burr hole. Nonspecifically activated splenocytes were lymphokine-activated killer (LAK) cells, both plastic-adherent and nonadherent, whereas specifically activated CTLs were either syngeneic (genetically identical) or allogeneic (genetically dissimilar). Syngeneic CTLs were T **lymphocytes** from Fischer rats **primed** in vivo with 9L cells and restimulated in vitro. Allogeneic CTLs were generated by exposing DA rat **lymphocytes** either to irradiated Fischer lymph node cells or to 9L Fisher tumor cells in vitro. Control groups included rats bearing 9L tumor who were untreated, those who received peripheral (i.p. or s.c.) administration of rIL-2, or those who received syngeneic unstimulated T **lymphocytes** and rIL-2. For a set of animals given the same inoculum of 9L tumor, significantly improved survival was shown for groups treated with nonadherent or adherent LAK cells (P less than or equal to 0.0003), syngeneic CTLs (P = 0.0327), or allogeneic CTLs (P = 0.0025) over untreated control animals by using Mantel-Haenzel nonparametric logrank equations. Only treatment with allogeneic CTLs **prevented tumor take**.

...and various effector cell populations in adoptive immunotherapy of 9L rat gliosarcoma: allogeneic cytotoxic T **lymphocytes prevent tumor take**.

Dec 1990,

... in the Fischer strain 9L rat gliosarcoma model. The in vivo cytotoxicities of nonspecifically activated **lymphocytes** and specifically activated cytotoxic T **lymphocytes** (CTLs) were assessed in a modified in vivo neutralization (Winn) assay. Effector cells (10(6...

... activated CTLs were either syngeneic (genetically identical) or allogeneic (genetically dissimilar). Syngeneic CTLs were T **lymphocytes** from Fischer rats **primed** in vivo with 9L cells and restimulated in vitro. Allogeneic CTLs were generated by exposing DA rat **lymphocytes** either to irradiated Fischer lymph node cells or to 9L Fisher tumor cells in vitro...

... p. or s.c.) administration of rIL-2, or those who received syngeneic unstimulated T **lymphocytes** and rIL-2. For a set of animals given the same inoculum of 9L tumor...

... untreated control animals by using Mantel-Haenzel nonparametric logrank equations. Only treatment with allogeneic CTLs **prevented tumor take**.

Descriptors: Brain Neoplasms--therapy--TH; *Glioma--therapy--TH; *Immunotherapy, Adoptive; *Interleukin-2--therapeutic use--TU; *T-**Lymphocytes**, Cytotoxic--immunology--IM

13/3,K,AB/13 (Item 13 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

06464065 90171604 PMID: 1968493

Effect of graft-versus-host disease on anti-tumor immunity.

Schreiber K L; Forman J

Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235-9048.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Mar 1 1990, 144 (5) p2018-26, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: CA09082; CA; NCI; CA41099; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BCL1, a spontaneous B cell leukemia of BALB/c origin, is rejected by

C.B-20 (Ighb, H-40b) but not BALB/c (Igha, H-40a) mice. Adoptive transfer of C.B-20 anti-BCL1 effector cells specific for the minor histocompatibility Ag H-40a protects irradiated C.B-20 but not BALB/c recipients. Because C.B-20 donor cells could potentially generate graft-vs-host disease (GVHD) in BALB/c recipients, we investigated the possibility that GVHD **prevents** the anti-tumor effect. GVHD was induced in (C.B-20 X B10.D2)F1 [H-2d, H-40b X H-2d,H-40b] recipients after injection of B10.D2-**primed** C.B-20 donor cells. GVHD was indicated by the histologic appearance of tissue sections from C.B-20----F1 livers, target organs of GVHD, which showed a marked mononuclear cell infiltrate around the portal tracts and central veins. In addition, splenic **lymphocytes** from these mice had altered CD4/CD8 ratios and were unable to respond to the polyclonal activators Con A and LPS. The mitogen unresponsiveness was at least partially due to the presence of a suppressor cell, because proliferation of normal spleen cells to Con A and LPS was suppressed upon addition of C.B-20----F1 spleen cells. Further immune dysfunction was evident by the inability of T cells from mice with GVHD to generate a CTL response to H-2 alloantigens. Addition of C.B-20----F1 spleen cells to F1 responder cells at the induction of culture did not prevent generation of CTL, indicating that a suppressor cell was not responsible for the lack of CTL activity. In this setting of GVHD, F1 recipients were able to reject BCL1 upon adoptive transfer of C.B-20 anti-BCL1 effector cells. These data indicate that GVHD-induced immune dysfunction does not inhibit the activity of antileukemia T cells.

Mar 1 1990,

...graft-vs-host disease (GVHD) in BALB/c recipients, we investigated the possibility that GVHD **prevents** the anti-tumor effect. GVHD was induced in (C.B-20 X B10.D2)F1 [H-2d, H-40b X H-2d,H-40b] recipients after injection of B10.D2-**primed** C.B-20 donor cells. GVHD was indicated by the histologic appearance of tissue sections...

... a marked mononuclear cell infiltrate around the portal tracts and central veins. In addition, splenic **lymphocytes** from these mice had altered CD4/CD8 ratios and were unable to respond to the...

Descriptors: Graft vs Host Disease--immunology--IM; *Leukemia, B-Cell--immunology--IM; *T-**Lymphocytes**--immunology--IM; Antigens, CD8; Antigens, Differentiation, T-**Lymphocyte**--analysis--AN; CD4-Positive T-**Lymphocytes**--cytology--CY; Cytotoxicity, Immunologic; Graft Rejection; Graft vs Host Disease--pathology--PA; H-2 Antigens--immunology--IM; Immune Tolerance; Immunity, Cellular; Immunization, Passive; Leukemia, B-Cell--therapy--TH; **Lymphocyte** Transformation; Mice; Mice, Inbred BALB C; Neoplasm Transplantation; T-**Lymphocytes**--cytology--CY; T-**Lymphocytes**, Cytotoxic--immunology--IM

Chemical Name: Antigens, CD8; Antigens, Differentiation, T-**Lymphocyte**; H-2 Antigens

13/3,K,AB/14 (Item 14 from file: 155)
 DIALOG(R) File 155:MEDLINE(R)
 (c) format only 2003 The Dialog Corp. All rts. reserv.

06056450 89135874 PMID: 2465081

Specificity of antigens on UV radiation-induced antigenic tumor cell variants measured in vitro and in vivo.

Hostetler L W; Romerdahl C A; Kripke M L

Department of Immunology, University of Texas M.D. Anderson Cancer Center, Houston 77030.

Cancer research (UNITED STATES) Mar 1 1989, 49 (5) p1207-13,

ISSN 0008-5472 Journal Code: 2984705R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

In vitro exposure of nonimmunogenic murine tumor cells to UV radiation (UVR) generates highly antigenic variants that are immunologically rejected by normal, syngeneic mice. The purpose of this study was to determine whether these antigenic variants cross-react immunologically with the parental tumor and whether the UVR-associated antigen unique to UVR-induced tumors is also present on the variants. Antigenic (regressor) variants and nonimmunogenic (progressor) clones derived from UV-irradiated cultures of the C3H K1735 melanoma and SF19 spontaneous fibrosarcoma cell lines were used to address these questions. In an in vivo immunization and challenge assay, the antigenic variants did not induce cross-protection among themselves, but each induced immunity against the immunizing variant, the parent tumor cells, and nonimmunogenic clones derived from UV-irradiated parent cultures. Therefore, the variants can be used to induce in mice a protective immunity that **prevents** the growth of the parent **tumor** and nonimmunogenic clones, but not other antigenic variants. In contrast, immunization with cells of the parental tumor or the nonimmunogenic clones induced no protective immunity against challenge with any of the cell lines. Utilizing the K1735 melanoma-derived cell lines in vitro, T-helper (Th) cells isolated from tumor-immunized mice were tested for cross-reactivity by their ability to collaborate with trinitrophenyl-**primed** B-cells in the presence of trinitrophenyl-conjugated tumor cells. Also, the cross-reactivity of cytotoxic T-**lymphocytes** from tumor-immunized mice was assessed by a 4-h 51Cr-release assay. Antigenic variants induced cytotoxic T-**lymphocytes** and Th activity that was higher than that induced by the parent tumor and nonimmunogenic clones from the UVR-exposed parent tumor and cross-reacted with the parental tumor cells and nonimmunogenic clones, but not with other antigenic variants. Furthermore, upon transplantation, the UVR-induced antigenic variants grew in UV-irradiated and immunosuppressed mice, but not in untreated mice indicating that the variants expressed the determinant recognized by suppressor T-cells present in UV-irradiated mice. These results demonstrate that highly antigenic cells generated by the in vitro exposure of two different murine tumors to UV radiation express a determinant shared with the parental tumor cells and nonimmunogenic clones, a unique variant-specific determinant and the suppressor cell-defined determinant present on UVR-induced tumors. Based on these results, two models are proposed to explain the make-up of the antigenic determinants present on the UVR-induced antigenic variants.

Mar 1 1989,

... cultures. Therefore, the variants can be used to induce in mice a protective immunity that **prevents** the growth of the parent **tumor** and nonimmunogenic clones, but not other antigenic variants. In contrast, immunization with cells of the...

... tumor-immunized mice were tested for cross-reactivity by their ability to collaborate with trinitrophenyl-**primed** B-cells in the presence of trinitrophenyl-conjugated tumor cells. Also, the cross-reactivity of cytotoxic T-**lymphocytes** from tumor-immunized mice was assessed by a 4-h 51Cr-release assay. Antigenic variants induced cytotoxic T-**lymphocytes** and Th activity that was higher than that induced by the parent tumor and nonimmunogenic...

; Cross Reactions; Mice; Mice, Inbred C3H; T-**Lymphocytes**, Cytotoxic --immunology--IM; T-**Lymphocytes**, Helper-Inducer--immunology--IM; Ultraviolet Rays

13/3,K,AB/15 (Item 15 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

05727031 88150871 PMID: 2964268

The augmentation of tumor-specific immunity using haptenic muramyl dipeptide (MDP) derivatives. III. Eradication of disseminated murine

chronic leukemia cells by utilizing MDP hapten-reactive helper T-cell activity.

Shima J; Yoshioka T; Nakajima H; Fujiwara H; Hamaoka T

Department of Oncogenesis, Osaka University Medical School, Japan.

Cancer immunology, immunotherapy : CII (GERMANY, WEST) 1988, 26

(1) p43-7, ISSN 0340-7004 Journal Code: 8605732

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A previous paper has demonstrated that enhanced tumor-specific immunity could be induced by priming mice with Bacillus Calmette Guerin (BCG) and subsequently immunizing them with syngeneic tumor cells modified with BCG-cross-reactive muramyl dipeptide (MDP) hapten. The present study establishes a tumor-specific immunotherapy protocol for a murine chronic leukemia based on the above T-T cell collaboration between antitumor effector T cells and anti-MDP hapten helper T cells induced by BCG priming. BALB/c mice which had been **primed** to BCG were injected intravenously (i.v.) with viable, syngeneic BCL1 leukemia cells. One week later, these mice were immunized intraperitoneally (i.p.) with unmodified or MDP hapten-modified, 10,000 R X-irradiated BCL1 cells, followed by 4 booster immunizations at 5-day intervals. The administration of unmodified BCL1 tumor cells into BCG-**primed** mice failed to **prevent** them from **tumor** death due to the persistent growth of preinjected BCL1 cells. In contrast, the immunization of BCG-**primed**, BCL1 leukemia-cell-bearing mice with MDP-modified BCL1 cells resulted in a high growth inhibition of leukemia cells and protection of these mice from death by leukemia. It was also revealed that potent tumor-specific, T-cell-mediated immunity was generated in mice which survived in this immunotherapy model. Thus, these results indicate that administration of MDP hapten-modified, syngeneic leukemia cells into leukemia-bearing mice which have been **primed** with BCG results in potent tumor-specific, T-cell-mediated immunity attributable to preventing the growth of disseminated leukemic cells.

1988,

... MDP hapten helper T cells induced by BCG priming. BALB/c mice which had been **primed** to BCG were injected intravenously (i.v.) with viable, syngeneic BCL1 leukemia cells. One week...

... booster immunizations at 5-day intervals. The administration of unmodified BCL1 tumor cells into BCG-**primed** mice failed to **prevent** them from **tumor** death due to the persistent growth of preinjected BCL1 cells. In contrast, the immunization of BCG-**primed**, BCL1 leukemia-cell-bearing mice with MDP-modified BCL1 cells resulted in a high growth...

... administration of MDP hapten-modified, syngeneic leukemia cells into leukemia-bearing mice which have been **primed** with BCG results in potent tumor-specific, T-cell-mediated immunity attributable to preventing the...

Descriptors: Acetylmuramyl-Alanyl-Isoglutamine--therapeutic use--TU; *Leukemia, Experimental--therapy--TH; *T-Lymphocytes, Helper-Inducer --immunology--IM...; Immunization; Immunization, Passive; Leukemia, Experimental--immunology--IM; Mice; Mice, Inbred BALB C; Neoplasm Transplantation; T-Lymphocytes--immunology--IM; T-Lymphocytes --transplantation--TR

13/3,K,AB/16 (Item 16 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

03210677 80022660 PMID: 226270

Concanavalin A-mediated in vitro activation of lymphocytes

primed against syngeneic SV40-induced tumor-associated antigens in mice into secondary effector cells capable of specifically **preventing tumor growth**.

Glaser M

Cellular immunology (UNITED STATES) Aug 1979, 46 (1) p201-7,

ISSN 0008-8749 Journal Code: 1246405

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Concanavalin A-mediated in vitro activation of **lymphocytes** **primed** against syngeneic SV40-induced tumor-associated antigens in mice into secondary effector cells capable of specifically **preventing tumor growth**.

Aug 1979,

Descriptors: Concanavalin A--pharmacology--PD; ***Lymphocyte**

Transformation--drug effects--DE; *Simian virus 40--immunology--IM; *T-**Lymphocytes**--immunology--IM

13/3,K,AB/17 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

08034658 Genuine Article#: 238ZP Number of References: 32

Title: T cell memory against colon carcinoma is long-lived absence of antigen (ABSTRACT AVAILABLE)

Author(s): Xiang R; Lode HN; Gillies SD; Reisfeld RA (REPRINT)

Corporate Source: SCRIPPS CLIN & RES INST,DEPT IMMUNOL, 10550 N TORREY PINES RD, IMM13/LA JOLLA//CA/92037 (REPRINT); SCRIPPS CLIN & RES INST,DEPT IMMUNOL/LA JOLLA//CA/92037; LEXIGEN PHARMACEUT,/LEXINGTON//MA/02173

Journal: JOURNAL OF IMMUNOLOGY, 1999, V163, N7 (OCT 1), P3676-3683

ISSN: 0022-1767 Publication date: 19991001

Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814

Language: English Document Type: ARTICLE

Abstract: Eradication of established colon carcinoma metastases is a major goal for adjuvant immunotherapy of this disease. This was accomplished in a murine model by targeting IL-2 to the tumor microenvironment with a recombinant Ab-IL-2 fusion protein (huKS1/4-IL-2). The generation of a long-lived protective immunity was demonstrated by a 10- to 14-fold increase in CTL precursor (pCTL) frequency and induction of genes encoding Th1 cytokines, followed by the generation of tumor-specific CD8(+) T effector cells, some of which differentiated into long-lived T memory cells. The frequency of pCTL correlated with enhanced immune protection against tumor cell challenge, and long-lived T cell memory was maintained in syngeneic SCID mice in the absence of tumor Ag. Tumor cell challenge of these SCID mice, concomitant with a boost of two noncurative doses of huKS1/4-IL-2 fusion protein, resulted in the generation of **primed** CD8(+) T effector cells with concurrent release of Th1 cytokines. These events culminated in the complete rejection of the **tumor** cell challenge and **prevention** of pulmonary metastases. Taken together, the data suggest that T cell memory against colon carcinoma can be maintained in the absence of Ag.

, 1999

...Abstract: two noncurative doses of huKS1/4-IL-2 fusion protein, resulted in the generation of **primed** CD8(+) T effector cells with concurrent release of Th1 cytokines. These events culminated in the complete rejection of the **tumor** cell challenge and **prevention** of pulmonary metastases. Taken together, the data suggest that T cell memory against colon carcinoma...

...Identifiers--TARGETED INTERLEUKIN-2 THERAPY; CANCER-IMMUNOTHERAPY;
IMMUNOLOGICAL MEMORY; **LYMPHOCYTES**; METASTASES; ERADICATION;
ELIMINATION; IMMUNITY; TURNOVER; CLONING

13/3,K,AB/18 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

07151101 Genuine Article#: 129JL Number of References: 42
Title: Induction of tumor-specific T cell response by cognating tumor cells
with foreign antigen-**primed** T-h cells (ABSTRACT AVAILABLE)
Author(s): Cheng TY; Wu JT; Lin RH (REPRINT)
Corporate Source: NATL TAIWAN UNIV, COLL MED, GRAD INST MICROBIOL & IMMUNOL,
1 SECT 1, JEN AI RD/TAIPEI//TAIWAN/ (REPRINT); NATL TAIWAN UNIV, COLL
MED, GRAD INST MICROBIOL & IMMUNOL/TAIPEI//TAIWAN/
Journal: INTERNATIONAL IMMUNOLOGY, 1998, V10, N10 (OCT), P1397-1406
ISSN: 0953-8178 Publication date: 19981000
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Sufficient CD4(+) T cell help is very important in generating
specific cytotoxic T cell responses. The inadequate activation of
tumor-specific T-h cells leads to failure of antitumor immunity. In
general, each individual consists of some **primed** T-h cells
responding to certain antigens, If these tumor non-specific pre-
primed T-h cells can provide sufficient help, the generation of
tumor-specific T cells may be enhanced. In the present study, we tested
this hypothesis by cognating and reactivating pre-**primed**
ovalbumin (OVA)-specific T-h cells with OVA-pulsed tumor cells which
could simultaneously present both OVA and tumor-associated antigen on
the same cell. We clearly demonstrated that immunization of
OVA-sensitized mice with OVA-pulsed P388 cells, but not unpulsed P388
cells, led to the induction of P388-specific cytotoxicity and tumor
resistance. Both CD4(+) and CD8(+) tumor-specific cytotoxic T cells
were detected in vitro, but only CD8(+) T cells played the major
effector role in **preventing** the growth of challenged **tumor**
in vivo. Taken together, our study demonstrated that the immunogenicity
of tumor cells can be enhanced effectively by cognating pre-
primed foreign antigen-specific T-h cells with tumor cells. These
findings have potential implications in developing methods to control
tumor growth.

Title: Induction of tumor-specific T cell response by cognating tumor cells
with foreign antigen-**primed** T-h cells
, 1998

...Abstract: h cells leads to failure of antitumor immunity. In general,
each individual consists of some **primed** T-h cells responding to
certain antigens, If these tumor non-specific pre-**primed** T-h
cells can provide sufficient help, the generation of tumor-specific T
cells may be enhanced. In the present study, we tested this hypothesis
by cognating and reactivating pre-**primed** ovalbumin (OVA)-specific
T-h cells with OVA-pulsed tumor cells which could simultaneously
present...

...were detected in vitro, but only CD8(+) T cells played the major
effector role in **preventing** the growth of challenged **tumor**
in vivo. Taken together, our study demonstrated that the immunogenicity
of tumor cells can be enhanced effectively by cognating pre-
primed foreign antigen-specific T-h cells with tumor cells. These
findings have potential implications in...

...Identifiers--CLASS-II MOLECULES; HUMAN NAIVE; B-CELLS; **LYMPHOCYTES**;
IMMUNITY; REJECTION; GENE; COSTIMULATION; TRANSFECTION; AUGMENTATION

13/3,K,AB/19 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

02387017 Genuine Article#: KY052 Number of References: 77
Title: **TUMOR-NECROSIS-FACTOR-ALPHA BLOCKADE PREVENTS NEUTROPHIL**
CD18 RECEPTOR UP-REGULATION AND ATTENUATES ACUTE LUNG INJURY IN PORCINE
SEPSIS WITHOUT INHIBITION OF NEUTROPHIL OXYGEN RADICAL GENERATION (Abstract Available)
Author(s): WINDSOR ACJ; WALSH CJ; MULLEN PG; COOK DJ; FISHER BJ; BLOCHER CR
; LEEPERWOODFORD SK; SUGERMAN HJ; FOWLER AA
Corporate Source: VIRGINIA COMMONWEALTH UNIV,MED COLL VIRGINIA,DEPT MED,DIV
PULM CRIT CARE MED,POB 50 MCV STN/RICHMOND//VA/23298; VIRGINIA
COMMONWEALTH UNIV,MED COLL VIRGINIA,DEPT MED,DIV PULM CRIT CARE MED,POB
50 MCV STN/RICHMOND//VA/23298; VIRGINIA COMMONWEALTH UNIV,MED COLL
VIRGINIA,DEPT SURG/RICHMOND//VA/23298; VIRGINIA COMMONWEALTH UNIV,MED
COLL VIRGINIA,DEPT PATHOL/RICHMOND//VA/23298
Journal: JOURNAL OF CLINICAL INVESTIGATION, 1993, V91, N4 (APR), P
1459-1468
ISSN: 0021-9738

Language: ENGLISH Document Type: ARTICLE

Abstract: Tumor necrosis factor (TNFalpha), both by direct action and by trafficking cells of the immune system, is implicated in cardiopulmonary derangements and PMN-mediated microvascular injury associated with gram-negative sepsis. We examined the effects of pretreatment with a monoclonal antibody to TNFalpha on PMN function, hemodynamic derangements, and alveolar capillary membrane damage in a septic porcine model. Anti-TNFalpha profoundly improved hemodynamic consequences in this model. Reduction in PMN CD11/18 receptor expression, lung myeloperoxidase activity, and attenuation of peripheral neutropenia (all $P < 0.05$) indicate that pretreatment significantly reduced lung sequestration of PMNs seen in septic controls. In contrast, PMN oxygen radical (O_2^-) generation was not significantly different from unprotected septic animals. Despite the presence of circulating PMNs primed for O_2^- burst, alveolar capillary membrane damage, assessed by bronchoalveolar lavage protein content and arterial PO_2 was markedly attenuated in the treatment group ($P < 0.05$). We conclude that anti-TNFalpha suppresses systemic hemodynamic actions of TNFalpha. Further, it prevents upregulation of PMN adhesion receptors inhibiting PMN/endothelial cell interaction. This prevents formation of a 'microenvironment,' protected from circulating oxidant scavengers, into which sepsis-activated PMNs release their toxic products. Pretreatment with anti-TNFalpha monoclonal antibody thus affords global protection in porcine Gram-negative sepsis.

Title: **TUMOR-NECROSIS-FACTOR-ALPHA BLOCKADE PREVENTS NEUTROPHIL**
CD18 RECEPTOR UP-REGULATION AND ATTENUATES ACUTE LUNG INJURY IN PORCINE
SEPSIS WITHOUT INHIBITION...

, 1993

...Abstract: generation was not significantly different from unprotected septic animals. Despite the presence of circulating PMNs primed for O_2^- burst, alveolar capillary membrane damage, assessed by bronchoalveolar lavage protein content and arterial...

...Research Fronts: REQUIRES COEXPRESSION; CULTURED RAT EMBRYONIC CNS CELLS)

91-0726 001 (ENDOTHELIAL LEUKOCYTE ADHESION MOLECULE-1;
LYMPHOCYTE HOMING RECEPTOR; ALLERGIC CUTANEOUS INFLAMMATION
INVIVO)

91-6294 001 (ACTIVATED NEUTROPHILS; REACTIVE OXYGEN SPECIES;
HYPOCHLOROUS...

?